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“ In adopting our title of the *Journal of Mental Science*, published by authority of the *Medico-Psychological Association*, we profess that we cultivate in our pages mental science of a particular kind, namely, such mental science as appertains to medical men who are engaged in the treatment of the insane. But it has been objected that the term mental science is inapplicable, and that the term mental physiology or mental pathology, or psychology, or psychiatry (a term much affected by our German brethren), would have been more correct and appropriate ; and that, moreover, we do not deal in mental science, which is properly the sphere of the aspiring metaphysical intellect. If mental science is strictly synonymous with metaphysics, these objections are certainly valid ; for although we do not eschew metaphysical discussion, the aim of this JOURNAL is certainly bent upon more attainable objects than the pursuit of those recondite inquiries which have occupied the most ambitious intellects from the time of Plato to the present, with so much labour and so little result. But while we admit that metaphysics may be called one department of mental science, we maintain that mental physiology and mental pathology are also mental science under a different aspect. While metaphysics may be called speculative mental science, mental physiology and pathology, with their vast range of inquiry into insanity, education, crime, and all things which tend to preserve mental health, or to produce mental disease, are not less questions of mental science in its practical, that is in its sociological point of view. If it were not unjust to high mathematics to compare it in any way with abstruse metaphysics, it would illustrate our meaning to say that our practical mental science would fairly bear the same relation to the mental science of the metaphysicians as applied mathematics bears to the pure science. In both instances the aim of the pure science is the attainment of abstract truth ; its utility, however, frequently going no further than to serve as a gymnasium for the intellect. In both instances the mixed science aims at, and, to a certain extent, attains immediate practical results of the greatest utility to the welfare of mankind ; we therefore maintain that our JOURNAL is not inaptly called the *Journal of Mental Science*, although the science may only attempt to deal with sociological and medical inquiries, relating either to the preservation of the health of the mind or to the amelioration or cure of its diseases ; and although not soaring to the height of abstruse metaphysics, we only aim at such metaphysical knowledge as may be available to our purposes, as the mechanician uses the formularies of mathematics. This is our view of the kind of mental science which physicians engaged in the grave responsibility of caring for the mental health of their fellow-men may, in all modesty, pretend to cultivate ; and while we cannot doubt that all additions to our certain knowledge in the speculative department of the science will be great gain, the necessities of duty and of danger must ever compel us to pursue that knowledge which is to be obtained in the practical departments of science with the earnestness of real workmen. The captain of a ship would be none the worse for being well acquainted with the higher branches of astronomical science, but it is the practical part of that science as it is applicable to navigation which he is compelled to study.”—*Sir J. C. Bucknill, M.D., F.R.S. (Journ. Ment. Sci., vol. vii, 1861, p. 137).*

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Part I.—Original Articles

THE TWENTY-FOURTH MAUDSLEY LECTURE: THE FUNCTIONS OF ELECTRICAL RHYTHMS IN THE BRAIN.

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THE deep pleasure with which I received the invitation to deliver this lecture was tinged with dismay, for as a physiologist I am only too frequently reminded that the contributions which psychiatry has received from physiology are, in fact, almost negligible. I was therefore bound to ask myself very seriously whether I could honestly accept the honour without committing myself to stray far beyond the confines of my own subject. Finally, I satisfied my conscience by deciding that the invitation was issued in the spirit of hope rather than satisfaction, and I trust that I shall not be misinterpreting the intentions of this Royal and learned body if I feel encouraged to develop a speculative rather than a purely empiric theme. My aim is to outline the manner in which the study of brain physiology may conceivably enable us to define the physical parameters of mental experience, and the title which I first suggested for the lecture was "The Frame of Reason." Vivid though the image may be for me, I admit that the more laconic title is better, for it does at least give us a landmark and a limit to our exploring.

I confess to a childish regret for the intricate ambiguities of my first choice of title, for ambiguity seems the keynote of cerebral function. It is no wonder that until a very few years ago the regions above the mid-brain were tacitly accepted as out-of-bounds to respectable physiologists. Few text-books of the last decade devoted more than 5 per cent. of their space to the cerebrum, and of this the great bulk was conditioned reflexes and clinical curiosities. Not that I wish to disparage either the school of Pavlov or the observations of the great neurologists—on the contrary, I can feel nothing but humility that it is to these prophets that physiologists must ascribe the authorship of their apocrypha.

The difficulty and the aforesaid ambiguities have, of course, quite a simple origin; whereas in the periphery, and even in the spinal cord, an experimenter can use his customary methods to ensure that he is studying systems with only

one or two variables, in the higher nervous regions he is faced by a multiplicity of simultaneous equations, and what is far worse, he cannot tell by inspection which are the dependent and which the independent variables. It is never obvious on which side of the experimental equation a term should appear, and as far as anyone knows, any term may continuously or intermittently influence or be influenced by any or all of the others.

This is clearly no easy field for the methods of classical physiology, and until the widespread adoption in recent years of electrical methods of observing the brain in intact human subjects, even the solid foundations laid by Adrian, Bremer, Dusser de Barenne, Lashley and their pupils, could not be used with confidence.

I should like to make quite clear at the outset that I do not attribute any unique theoretical importance to the *electrical* nature of the cerebral events which are recorded in the electroencephalogram. It is another handicap which we must bear as best we can, that our companion-in-arms, the biochemist, cannot accompany us in our raids on this redoubt—his weapons are still too slow and deadly to help us to bring back our facts alive. There still seem to be some echoes of the notorious dispute as to whether nervous activity should be considered as electrical or chemical in nature. This seems as unrealistic to me as to debate whether a torch battery should be sold in a chemist's shop or an electrician's; any chemist would be astounded at the notion that a chemical reaction could occur without electronic change and, though it is true that electricity *can* be generated without chemical reaction, as far as I know no electrophysiologist would maintain that the electrical energy of nervous impulses is generated by the movements of magnets or by friction between insulators. I am perfectly willing to accord to acetylcholine or any other reasonable candidate an importance as great as that of the compounds in a Leclanché cell—and would ask the biochemist to agree that a nervous impulse is more chemical than a lightning flash, more electrical than an oil lamp, and leave it at that for the time being.

Now, before I launch into the main topic of this lecture, the function of the rhythmic electrical activity of the brain, may I for a moment try to define in simple numerical terms, the scale of the problem which we seem to be tackling. It is said that in the human brain there are of the order of ten thousand million nerve cells. We have no *a priori* right to assume any limit to the permutations of interconnection of these units and if, in order to achieve concise results, we must really try to think and work on this fantastic scale, then clearly we had better give up trying to consider this subject as anything but a charming diversion from everyday reality. These great numbers have of recent years been rather irresponsibly quoted in comparison with artificial machines to give an idea of brain complexity and it is true that the permutations of 10^{10} set an upper limit, but, of course, it might as well be infinity. What the working experimenter wants to know is the *least* difficulty he can hope for; no one had the audacity to sail into the outer ocean as long as the world was believed flat; we can tolerate a boundless sea, but not an infinite one.

I have tried to set down, therefore, without presumption of truth, still less of finality, what may be the lower limit of brain complexity, much as an idle

Aristotelian may have done, or a list-loving schoolboy. We may add up the functional effector units—joints, glands and so on—controlled by the brain and multiply this by the degrees of freedom which they seem to possess and in this way get a crude estimate of the number of things the body can be made to do; it seems to be only about 500. The same arithmetic applied to the receptor field gives about the same number, though for different reasons, so we can conceive of a machine with about 1,000 functional control elements which would seem to an observer to have the same capabilities as a higher animal. The list would be a good basis for the performance specification of a robot. Oddly enough I understand that the greatest number of nerve-cell patterns discerned as cortical regions is also about 500—an encouraging coincidence.

The question now arises, would such a machine be likely to exhibit any of the general behavioural properties of an animal, or would it be just a carcase which would twitch appropriately when pinched, a spinal cord?

The answer depends upon the rules which govern the ways in which the control elements can be interconnected with one another; a thousand reflex arcs is a reflex arc multiplied by a thousand. But if one grants that in any pair of these elements each unit may be dependent or independent or interconnected with the other in any way, the picture changes, for two elements alone can exist in any of six possible modes and 1,000 in nearly one thousand million. We have extracted a large number again, but it is the dynamic result of a permutation, not the start of one. Each of these permutations will be unique and theoretically recognizable, for the sum depends upon the assumption that all the elements can interact on one another in specific ways, though we have postulated nothing so far as to how these interconnections may be established or varied.

In order to study this abstraction more easily, models have been built containing only two elements connected with two receptors, one for light and one for touch, and two effectors giving progress and rotation, with various possibilities of interconnection. This device is in the nature of a toy rather than a tool and reminds one of the speculations of Craik and the homeostat of Ashby. To the latter it bears roughly the relations of a tortoise to a lettuce leaf, since it is mobile and exploratory rather than sessile and ultrastable. It is entertaining to consider what would happen if the homeostat were arranged to signal its stability by a pattern of lights and the wandering toys were allowed to browse on the illuminations which signal the current they require; would the capacity of the homeostat for internal reorganization or the predatory persistence of the tortoise win the day—or would the two find a condition of mutual toleration?

Frivolity apart, this device has yielded several valuable lessons. First, that with only two elements, behaviour is exceedingly complex and quite unpredictable when the device is operating in a normally irregular environment. Second, that, given a single inherent rhythm whereby the photoreceptor continually scans the environment, and a persistent mobility, sooner or later the whole environment is tirelessly and meticulously explored. Third, that by using a positive feedback or regenerative circuit set in operation by a tactile stimulus, the sensitivity to distant lights can be entirely subordinated to the

need for circumventing immediate material obstacles, and at the same time the oscillations generated can be used to help the device to butt its way through small obstacles or sidle around large ones. Fourth, that, still with only two elements, moderately bright lights can be made attractive, brighter ones repulsive, so that the device can avoid the fate of a moth in a candle—otherwise it would merely seek the sun—yet never move too far from the lamp which signalizes its source of current. Fifth, that by connecting a source of light with the effector which is inhibited by light the device can be made to execute a specific ritual of behaviour when it detects its own reflection in a mirror or from a white surface, since in these circumstances it will set up an oscillation in a special mode, which includes the environment as a part of the reflex circuit. Sixth, by reason of the scanning mechanism already referred to, the model can avoid the dilemma of Buridan's ass or Dante's free man, "*intra due cibi*," for if two lights of equal intensity are present at equal distances from the model it will not seek a point equidistant between them and "*morria di fame*"—as many animals acting tropistically do in fact do—but will visit first one and then the other. Finally, it has been found desirable to incorporate two of the simple operations used in most nervous systems, partial differentiation and later integration, giving the device a heightened response to rapidly changing stimuli, but appreciation of steady states at a high level of intensity, combined with a short-term memory sufficient to get it well away from an obstacle before it renews its exploration or seeks its distant goal.

The social behaviour of these machines, though possibly relevant to the wider aspect of this subject, I will leave to another occasion—sufficient to mention that they display many of the paradoxes which plague our own community.

I hope that this detour into a private fancy does not seem too irrelevant to you; I would only establish, at least for the sake of argument, whether or not the physiological exploration of the mind is doomed to early shipwreck on some already charted reef. It seems to me important to realize that of the many features of the mind and behaviour which are quoted against mechanistic philosophies, there are some at least which are easily mimicked by machines. Exploration, curiosity, free-will in the sense of unpredictability, the seeking of goals, self-regulation, the avoidance of danger, a scale of values and relative importance, self-recognition, the avoidance of dilemmas, foresight, memory, learning, forgetting, association of ideas, form recognition, original creation and the elements of social organization are all within the capacity of purely mechanical devices, and the responsibility seems to me to rest now with the transcendentalists to define some further aspect of behaviour or experience for the other side to attempt to reproduce. You will notice that I have not quoted in support of psychic mechanism the large computing engines which are sometimes called electronic brains. These are not toys or pets, but tools, implements not models, and presumably the better they follow their instructions, the better pleased the designer will be, and the less they mimic the antics of the "wandering lunatic mind" the more useful they are to a mathematician. They achieve great speed, accuracy and fidelity by using vast numbers of electronic relays. That they do their sums by chattering "one and one and

one and one . . . " would delight the creator of the White Queen, but their sheer speed and certitude makes them seem very unlike the only brain with which I am personally acquainted. These big adders are prodigal where our toy is parsimonious in the extreme, and I find this principle of parsimony as prominent in the world of organisms as it is helpful in the realm of ideas—Occam's razor is as sharp in the struggle for existence as it is in wordy strife, and my justification for alluding at all to the toy is not that it does anything particularly well, but that it does anything at all with so little.

If we transfer our playroom impressions to the arithmetic of cerebral elements, we must recall that the relevant comparison is not between 2 and 1,000, but between 6 and nearly 1,000,000,000, and I challenge any sceptic to prove that the ratio of behavioural complexity between toy and man is greater than 1 to 100 million.

But the construction and design of these models does more than give us perspective—it helps to give us an idea of what sort of functions we should be on the look-out for in studying the restless groping brain; this seems more hopeful than to approach the problem from the other side, for our success in assigning functions to the electrical activity we have observed does not seem to have been conspicuous. It is easier to find a needle in a haystack if you know what the needle should look like—and that is about the scale of the matter.

You will notice that I am veering a little toward what is now called the Cybernetic discipline, that is, a fashion of thought which permits consideration of living and mechanical systems as one species in so far as they possess similar properties, with particular relation to their capacity to direct themselves toward a goal. I make no apology for this, since I believe it may help to make clear some of the observations and speculations to follow, but I need hardly say that in my use of any such operational analogy I insert mentally in every metaphor and simile the important sign "as if." We sometimes find it convenient to put the mechanical cart before the living horse when the load is too great for the poor beast and there is a chance of a tow.

What functions then, do our models and our knowledge of behaviour suggest that a brain should have if it is to be more than a super spinal cord? On the sensory side first, you will recall that in order to give a model a propensity to explore and search for stimuli, we had to provide a mechanism whereby its single light receptor could scan the whole environment repeatedly. The internal connections are so arranged that whenever the receptor receives an adequate stimulus, its scanning is halted and at the same time the rotatory movement of the whole organism is checked, so that it progresses by a series of diminishing cycloidal movements toward the source of light. The only alternative is to provide a large number of receptors facing in all directions, with a correspondingly elaborate system of motor control. This arrangement gives no better results and is extremely wasteful of space and power and more liable to break down in proportion to the increased number of components. Applying the principle of parsimony then, we should expect to find in the space receptor sections of a brain, mechanisms whereby the sensory fields could be scanned continuously in such a way that the detailed bits of information they contain could be conveyed to a central assembly by only a few channels, there to be

related one with another for appropriate action to be taken. Otherwise every single receptor unit would have to be represented by a branching chain of brain elements to connect it with all other possible elements up to the highest level—and this we know, in the case of the brain, cannot be the case. Now, the characteristics of such a scanning mechanism would be that its range or amplitude of activity would be greatest in the absence of a signal, when it would be regular and rhythmic, sweeping over the featureless central projection of the sensory organ as smoothly as the electron beam of a television camera scans the image screen for the picture elements. But on the instant that a signal appeared on its beat it would be halted, and its position at the check would convey to all other regions the relative position of the detail of sensation. When a complex pattern appeared, the succession of runs and checks would repeatedly convert a spatial pattern which was constant during the time of a single sweep—a frame, as the television engineers call it—into a series of signals on a base of time, so that all the information contained in a single parameter of sense can be conveyed on a single channel in a code of unit pulses. The economy effected by this means can be gauged by the saving in a television system, in which the scanning process transmits on a single radio channel information which would otherwise require over 100,000 channels—since the specifications of a television set are designed to fit the acuity of our own senses, this economy factor may well indicate the *lower* limit of saving which our own brains should obtain from a space-time transformation of this sort.

But what is the price of such parsimony? First, reception speed will be limited to the frame frequency; changes in space which occur more frequently than this or movements which cover an appreciable distance in the time of one frame will lead to blurring and distortion of the pattern. Second, intermittent signals which are shorter than the duration of the sweep but recur at about its frequency will give the illusion of movement. Third, a special mechanism must be devoted entirely to the generation of the scanning sweep, and also, if action is to be taken on the basis of information received from the field scanner, to ensuring that executive orders are transmitted to effectors only at such moments as the sensory data are complete; that is, the outflow of centrifugal messages must be to some extent regulated by and synchronized with the time base on which the centripetal ones are coded.

Now, if we consider vision as a representative of the space analysing senses, what evidence can we find of these properties? From the anatomical standpoint there seems to be progressive reduction in the number of units allotted to the receiving channels as we move from the retina to the projection and association areas. The psychologists have known for many years that a pattern cannot be recognized in less than about one tenth of a second, and that a motor response to a visual signal has a surprisingly long and inexplicably variable latency—from 100 to 200 milliseconds. Recently we have studied in some detail the subjective sensations produced by a flickering stimulus in which each flash is infinitesimally short on the time scale we are using, and in which there is absolutely no movement of the light during illumination and extinction. I shall be describing in some detail the results obtained with this method, but it is relevant here to mention that the principal feature described by all subjects

is a vivid appearance of movement. Since there is no objective motion, this effect must be due to a movement of something between the eye and the integrating or "perceiving" level of the brain. And then, of course, we have the alpha rhythms of the EEG, and the cat is out of the bag—a transparent bag I fear, for the direction of my argument has been quite obvious—but I was anxious to show that the existence of some such rhythm could be predicted without recourse to electronic gadgets from facts which have been known for over a generation—if only someone had predicted it 25 years ago!

The alpha rhythm, unexpected, unwanted and disinherited by physiologists, is now familiar enough, but although it attained its majority this year, we still do not know as much about it as we should if we are to condone its origin on the wrong side of the biological blanket. That its name was bestowed by a psychiatrist and not by a physiologist may, of course, be a handicap, but let us see whether we can find in this phenomenon at least some capacity for doing useful work.

Some seven years ago we began to study this among other electrophysiological rhythms with the aid of an automatic analyser which I thought might throw some light on the otherwise mysterious fluctuations which it displays in most people, and we also hoped to discover the reason for the equally large and puzzling differences between individuals. The first suggestion which the analyser made was one which I had half expected—that the rhythm is plural. In the great majority of normal subjects the analysis showed not one component but two or three, all in the same band of frequencies, 8–13 c/s, and located more or less in the occipital region, but individually responsive to various stimuli, and, with special care, referable to distinct domains within the visual and visual-association areas. In many people—those with a classical, large amplitude, responsive rhythm—one component is much larger than the others in conditions of visual and mental rest, but even in these, when the attention is more alert, the composite nature of the rhythm can easily be recognized. For technical reasons which I need not elaborate, I was sceptical of this finding until I was assured that the components revealed by analysis could actually be tracked down and identified by residence and occupation as well as by frequency. More recently my doubt has been reduced still further by confirmation from two other sources—Cohn in America, who made exact direct measurements of frequency in high speed records, and Kensuke Sato of Japan, who analysed records by an unrelated mathematical method. Both these experimenters concluded that in most of the records they had studied, two or more components must have been present. As a working hypothesis, then, we may reasonably consider that in the transformation of a visible pattern of light into a "percept" or significant mental event, several rhythmic processes are concerned. Further, when a pattern is recalled or imagined, one or other or all of these rhythms may again be involved. At the suggestion of Golla, whose interest in these possibilities is, of course, older than the alpha rhythms, we studied the question of imagination in some detail, since it seemed at the root of the differences between individuals. This began some years ago and the early results are probably familiar to you, so I need not recount them in detail, but in general we found, and continued observation has

confirmed our early impression, that in persons who habitually employ vivid and plastic visual images for mental tasks, images with all the luxury of colour depth and movement—in these the alpha rhythms were never continuous and the analyses were complex and variable—it is necessary to average the alpha analyses over a period of two minutes or so before the pattern begins to repeat in the graph. This gives some idea of the variation in the imaginary repertoire, for people of the opposite type, those who never, or only with great difficulty, employ visual images, give analyses which are almost identical every ten seconds or less. I feel that this time-function of variance may be a useful measure to apply to the analysis of personality; since it can be done automatically, it is easy to collect the information and it does seem to have a real meaning when applied to imagination. Although the parameter is a rather derivative one the measure has the advantage that it is a simple number—the shortest interval over which analyses can be made, so that successive analyses are superimposable within, say, 10 per cent. Such studies are, of course, unsatisfactory in the sense that they take little account of what the images concerned actually are; they indicate the order of richness or variety, but not the manner in which any particular mental event is related to any electro-physiological one; we shall see later that this correlation is far from ridiculous, but must be studied by a different method.

We therefore embarked upon another line of study, complementary to the first. We know that the aspects of a mental experience in the field of vision have unique properties—the beginning and the end—when a light is suddenly turned on in a dark room a subject shows not merely a blocking of most of his alpha components, but also a brief “on” effect, evoked in the occipital region. In some subjects this evoked potential is very small, as seen in the conventional EEG, but it can nearly always be identified by analysis of some sort. The latency of the evoked potential seemed variable at first, but the more careful the technique the shorter and more constant it becomes. Gastaut, using electrodes in the brain, and Cobb using a special display method, have shown that it is certainly less than 50 msec. and probably much less—in any case it is very much shorter than the time taken for the alpha rhythm to die away when the stimulus is a prolonged one and is only a small part of the total reaction time when a movement has to be made in response to the stimulus. This is important, because it means that, as predicted earlier, if a scanning process is involved in visual perception, an additional and variable delay is one of its drawbacks. In our toy model, if a light is turned on just after the scanning device has passed the position of the light, a complete rotation and extra delay must elapse before the scanning is checked and a response is elicited. It is not surprising therefore to find that though the first sign of the evoked response is constant in time, the later events are very variable both in one individual and between individuals. In our early experiments, four years ago or so, we were delighted to find—though I suppose a physiologist should have been horrified—that one of the factors which controls the latency, form and amplitude of these later events is the state of the subject’s mind. Seen in its simplest form the effect is as follows: When a subject’s eyes are illuminated by bright short flashes of light, the evoked response can be seen either in the

primary record or in the analysis. In the latter particularly the amplitude and detail of the spectrum may remain constant over a long period. But if the subject is asked to make some mental effort which is known to involve visual imagination, not only is some alpha component blocked, but the evoked response, which may be at a frequency quite different from that of the alpha rhythms, is much reduced in amplitude and altered in appearance. In the analysis, the change in form is usually seen as a relative increase in the proportion of activity at frequencies which are multiples of the stimulus rate. This suggests that those cerebral regions which were previously responding regularly to the external stimuli are mobilized for internal service when the attention is directed to an imaginary problem—it is possible, therefore, that imagination involves the projection of an internally constructed assembly of data upon the same area as is otherwise used for the processing of “real” or external information, before the pattern can be recognized and used for the miniature experiment of thought.

We have devoted some time to studying this hypothesis and since the experiments are far from complete—there are many technical complications—my account must be tentative, but briefly, it seems that the response in the primary projection visual areas at the frequency of the stimulus is in fact at the disposal of both external and internal authorities. One may ask, how, then, is it possible to distinguish between real and imaginary events, as many of us seem to do? It is conceivable that this is done by a signal from the very first component of a response evoked by an external stimulus—setting all the switches to “real” so to say; if this preliminary warning is faint or missing altogether we tend to assume that the situation is imaginary. Since the elementary evoked response is small for indistinct or slowly changing stimuli there might be difficulty in deciding whether such were real or not, and indeed, who has not avoided imaginary figures on a dark night? Of course, the other senses are commonly used to check the evidence of the eyes, but one should recall that when straight lines are made to seem curved with prismatic spectacles, the proprioceptors of the arm can often be inveigled into *feeling* them curved, and into following the over-compensation after the spectacles are removed—visual data are not merely dominant but almost dictatorial. What, then, of those people who fail to recognize that their images are different from external stimuli? Any failure of the process whereby incoming signals are used to preclassify their consequences would, of course, give this effect, and it may be significant—if true—that in individuals with visual hallucinations the elementary evoked responses seem particularly small and in those with consistent delusions they are fantastically distorted and widely dispersed both in time and in brain-space. This brings me to another of the peculiarities of the responses evoked by visual stimuli. You will recall that a scanning system such as we suggest as a function for the alpha rhythms must have certain weaknesses. We realized very early on that the technique of using rhythmic stimuli was a powerful method of identifying those faults. The subjective impression of movement and pattern is, of course, one, but we were much intrigued to find in our earliest experiments that it was by no means only visual illusions which were evoked by flickering light. A few moments ago I

mentioned that one of the effects of mental effort on the evoked responses was a change in their form and harmonic content. The peculiar thing about these harmonics is that they are not invariably—or even usually—in what are generally regarded as visual areas. They may, in fact, appear in almost any part of the brain. Study of their magnitude and distribution relative to the fundamental response is empirically useful in studying organic brain disease, because when they are exaggerated in an area which would be expected to show a fundamental response or nothing, we often find a serious disturbance somewhere nearby in the neuroanatomical sense. This, taken with their augmentation by mental effort suggests that activity at multiples and submultiples of a given primary process may be used to convey information about that process to distant regions of the brain in such a way that its provenance and destination are both included, so to say, on the label, and delays and misdirections are less likely. I sometimes consider activity in harmonic modes as a sort of cerebral gossip. The links in this argument are, I admit, tenuous, but one quite important inference from it can be made, and the verification of this has led to rather suggestive results. If the frequency as well as the pattern and position of a cerebral process are important, then it should be possible to insinuate into a receiving area what would seem to be an important message from another region merely by making the transmitting region active at the correct frequency. It might not be possible to predict what the message would mean, but if some action resulted, its acceptance could be assumed. An analogy that suggests itself is derived from cryptography. If one believes that one has discovered part of an enemy code or cipher and wishes to test one's inference, one method is to send a succession of messages to the receiving station using such symbols and patterns as one thinks one has recognized. If the recipient seems to regard these as anything but nonsense one may feel some confidence that so far at least one's assumptions are justified. If certain groups result in violent and otherwise inexplicable action one can feel even greater satisfaction.

This may seem fanciful, but in fact this is precisely what we have found to happen. In our early experiments many subjects exposed to a flickering light spontaneously described bizarre non-visual sensations and what pleased us more, whenever they did so, the brain area generally assumed to be connected with the sensations described became electrically active, either at the stimulus frequency or at a multiple or submultiple of it. Many of these findings have already been published and I only wish here to reiterate the general inference that by activating a sensory area at the correct frequency by physiological stimuli, it can be forced to communicate with other regions in a way which suggests that the frequency and rhythm of the activity is of prime importance. If rhythmic physiological stimuli were of frequent occurrence this property would certainly be a very serious fault, but in natural conditions the eye at least is not often exposed to regularly flickering light—the effect *is* sometimes seen as a natural fault, for several patients have told us of seizures induced by accidental flicker; perhaps some would consider the specific and violent excitation of the whole body evoked by rhythmic auditory stimulation as a fault—certainly it is regarded by many as agreeable and by some as indispensable. The Greek school masters considered dancing as an essential part of education,

together with music and mathematics, though they wisely prohibited the use of more than two sources of rhythm at once.

The transactivation effects which we observed at first were intermittent and apparently arose at random ; it was some time before we realized that their occurrence was not entirely haphazard but determined by the mental condition of the subject. We found, for example, that if there was a tendency for stimulation at 12 f/s to evoke a large component at 12 in the occipital region and others at 6 in the temporal and 24 c/s in the frontal area, the proportion of these subharmonic and harmonics was influenced by the attitude of the subject to the experiment. Whenever the 6 c/s component appeared there would be a subjective report of emotional perturbation and dizziness, while the 24 c/s was associated with intellectual analysis of the illusory visual patterns provoked by the flicker. Furthermore, if the subject were encouraged to abandon himself to the emotional tide, or still more if further emotional aggravation were added, in the form of embarrassing remarks or questions, the temporal 6 c/s component would swell until it out-topped its fundamental and sometimes the subject would refuse to continue, complaining of an intolerable affective state. On the other hand, if the atmosphere were maintained on an intellectual level with questions about the detail of the visual illusions and so forth, the anterior high harmonics would be augmented. In either case, when the stimulus was withdrawn both electrical and subjective effects disappeared almost at once.

Usually there was a short after discharge, lasting a fraction of a second. The significance of this after-effect will be appreciated when it is mentioned that its frequency was often not precisely that of the stimulus, for this means that our rhythmic stimuli were not merely evoking a series of discrete responses at precisely their own frequency, but were setting into oscillation a mechanism already present in distant areas, with its own frequency, domain and subjective correlate. Here is further evidence that the receiving area is, in fact, prepared to accept messages in the code presumed, and deal with them in its own way. In some cases two or more effects can be observed simultaneously : in one normal subject for example, the combination of intellectual analysis and spontaneous emotional rejection during stimulation at 13 f/s increased simultaneously a temporal subharmonic in the theta band at 6-7 c/s and a harmonic at 26 c/s in the frontal region, while it reduced the amplitude of the fundamental response at 13 c/s. The inexorability with which certain regions will pick out from a stimulus whatever aspect of it seems to suit them is illustrated by the fact that in some subjects activity in the theta band will appear in the temporal lobes—with emotional and kinaesthetic disturbance—when the stimulus frequency is within that frequency range *or* multiples of it, *or* varied in frequency in such a way that the *difference* between the upper and lower limits of variation is equal to 5 or 6 (e.g. from 10-15 *or* 12-18 c/s), *or*, when two rhythmic stimuli are present together, when either frequency is correct, *or* when their differences *or* sums are correct. Indeed, the effects of two simultaneous sources are so peculiar and generally disagreeable that one can understand the Hellenic moderation in this matter.

Not all the variations in the response are under the control of subject or operator. Spontaneous fluctuations in mood have a profound influence in the

same direction and to the same extent as short-term changes in attitude. Subjects who are accustomed to the procedure and its results soon come to be able to foretell quite accurately what their response will be from day to day, according to their subjective assessment of their spirits. Fatigue also has a great effect, which is diminished by drugs used to alleviate or postpone fatigue.

For some time we assumed that the frequency of the secondary and distant responses was strictly related to that of the stimulus, though the Russians, Livanov and his colleagues had reported otherwise. The observation that harmonics particularly, and after-discharges, when they occurred, were not precisely frequency-linked, aroused our suspicions and careful measurements have shown that there is frequently, in fact almost always, some slight discrepancy between stimulus and response rates. Even when, using a recently improved method of instantaneous frequency indication, one attempts to synchronize the stimulus precisely with that of an evoked secondary response, there is an exasperating backlash and jitter. This, of course, is further evidence of the pre-existence of the activated mechanisms, but makes it difficult to maintain an activation for long periods. Usually the response becomes slower as it increases in amplitude, but the effect is sometimes more intricate.

In order to lock the stimulus more firmly to the chosen cerebral response, various experiments have been made with electronic devices by which an evoked response could be made, so to say, to press a trigger which would release a stimulus to evoke a further response and so on. The important feature is that the delay between striking the cap and firing the charge must be controllable smoothly and over rather a wide range. Shipton has developed a system which performs this function admirably, and this has the further advantage of having two barrels, as one may say, to fire two stimuli at any interval apart. With this accessory the brain of a subject can be encouraged to build itself up into a really impressive oscillation, which in some cases, runs away and leads to a convulsive breakdown of all control. Before considering the application of this system to purely psychiatric problems, I should here digress for a moment and take you along the other route by which our present position was reached—the study of epilepsy.

The starting point was a purely practical one of diagnostic efficiency. As everyone knows, dramatic though the electrical discharges in true epilepsy may be, an obstinate proportion of confirmed epileptics have resting EEG records which are either normal or non-specifically abnormal by any criteria. This irks the electroencephalographer, and one of the earlier applications of frequency analysis was to this problem. We immediately noticed that the resting analyses of patients with a history of seizures, particularly *petit mal*, frequently looked different from normal ones even when the resting records were uninformative—there seemed to be a wide distribution of activity in clumps all up the spectrum. Of course, when we analysed during wave and spike paroxysms we obtained spectra showing many components which were harmonically related or nearly so. This is inevitable and not necessarily significant. We also showed what is again to be expected, that a convincing copy of a wave and spike pattern can be synthesized from harmonically related components in the correct relations of amplitude and phase. We went a step

further and demonstrated that when the same components were generated in different parts of a model head and electrodes placed on it as for an EEG, some channels would display the wave and spike, others quite different wave forms, according to the size and phase relations as seen by each channel. Frequency analysis of such synthetic records, of course, since it takes no account of internal phase relation, gave a similar spectrum whatever the form of the recorded pattern.

All these facts suggested that one should examine the many-banded spectra of resting epileptics more closely and we therefore attempted, in as many cases as possible, to locate and delimit the various components and to correlate them with the spatial and frequency analyses during a "wave and spike" episode in the same case. The results strongly suggested that in most patients the seizure pattern was the resultant of many of the widely spaced resting components, synchronised and augmented by one of the slower rhythms. On the basis of this it was found statistically justifiable to predict the appearance of a diagnostic seizure pattern from the appearance of frequency spectra, though in some cases the prediction was not fulfilled until several very long records had been taken. I then went so far as to suggest that the liability to minor attacks was due to the unfortunate presence of a set of numerically related electrical rhythms in one brain, and the onset of a particular attack to the exact synchronization of these rhythms by the appearance of some large slow rhythmic component. I suggested that the well known effects of over-breathing alkalosis in *petit mal* were due to synchronization by the large slow waves which it evokes and which are not in themselves peculiar to epileptics; sleep too, with its slower rhythms I thought should act as a convulsant. I further predicted that any agency which evoked an adequate electrical response at a frequency which was a multiple of some of the inherent resting rhythms of an epileptic should evoke a convulsive discharge.

This was just before I decided to use modern electronic methods of visual stimulation for other purposes and it was not until we had witnessed the complexity and wide variation of the evoked response in many normal subjects that I realized how powerful the method might be when applied to the testing of my prediction.

The first subject on whom the method was tried was one whom we had followed for some years, and whose wave and spike characters had been well analysed. They always began with an augmentation of the 8 c/s resting rhythm. However, stimulation at 8 f/s was ineffective, so we tried at 16, but without result. We then connected the stimulus lamps to our first trigger device, which was a crude affair but did ensure synchronization of stimulus and response. Thanks to the patience and dexterity of my wife, it was found that when the flash was locked first to the 16 c/s component of the parietal resting record for a few seconds and then immediately to the 8 c/s occipital one, a wave and spike pattern invariably followed. This was the first patient in whom a seizure discharge was evoked by rhythmic stimulation, and it is amazing that it succeeded, because we have since found that the key to fit this lock exactly is one of the most intricate of all the hundreds we have had to fashion.

I have related this anecdote to show that the connection between the evoked responses and mental state of relatively normal people on the one hand, and the dramatic features of epilepsy on the other did not immediately impress us; the first was a sort of experimental metaphysiology, the second a strictly practical development of clinical electroencephalography. But as the number of epileptics who responded to photic stimulation mounted toward the thousand mark in our files, we began to be impressed by the similarity between the records just before activation of a seizure pattern and the more subtle and evanescent features which we had earlier seen during "psychic" activation of normal subjects. The principal resemblance is the tendency for a discharge to appear in the fronto-temporal region at a theta subharmonic of the stimulus frequency when this is between 10 and 20 per second (Fig. 1). In an epileptic, when the stimulus is terminated in this preliminary stage it is not unusual for there to be a complaint of feeling queer and unreal, and some patients will volunteer that they have had a feeling exactly like the aura which usually precedes an attack.

That activation of a normal brain area should resemble an epileptic aura is not in the least surprising, since this may well be its nature, but we began to wonder whether the process could not be carried a step further, whether something like an epileptic seizure could not be induced in a non-epileptic by trying every possible combination of stimuli condition. I should perhaps interject here, that even in epileptics there is often only one set of conditions in which photic activation can be obtained with regularity. In some cases, for example, it is necessary to turn the stimulus on just at the moment when the eyes are closed; there is no effect with the eyes open or closed, whether the stimulation is continuous or intermittent, but for perhaps one second as the eyelids shut, the brain is in a condition to generate a wave and spike when the flash also starts just then and is at the right frequency (Fig. 2). In other epileptics it is necessary to provide a conditioning process of flashes at a high frequency for some minutes before seeking for the effective rate of stimulation, after which the response becomes brisker and larger with each exposure. In others, again, the response fades away smoothly after half a dozen repetitions (Fig. 3). So we foresaw that even if it were possible to provoke a paroxysmal discharge in a non-epileptic it would involve tedious trial and error, since we would not necessarily have an idea of what the important factors might be.

One of our first partial successes was in the twin sister of an epileptic—partial in that she was a monozygotic twin and such individuals do often show electrical signs of epilepsy even when the personal clinical history is negative (Fig. 4). In this case the epileptic twin responded instantly at 12 f/s with regular frontal spikes and violent myoclonic jerks, though she had never had a myoclonic seizure. This is one of the activation types which we recognize now as fairly common. The non-epileptic twin responded in an identical manner, at the same frequency and after the same latency, with the same subjective sensations and even more violent jerks. This was encouraging, but it was not long before a more startling case fell into our hands. In this patient there was no history of seizures, nor has prolonged observation revealed anything of an epileptic nature, though there are certain patho-physiological features

which will be mentioned later. She, also, responded with extremely large frontal spikes and violent jerks when the flash frequency was between 8 and 12 f/s (Fig. 5). She found the experience most disagreeable and since she was in

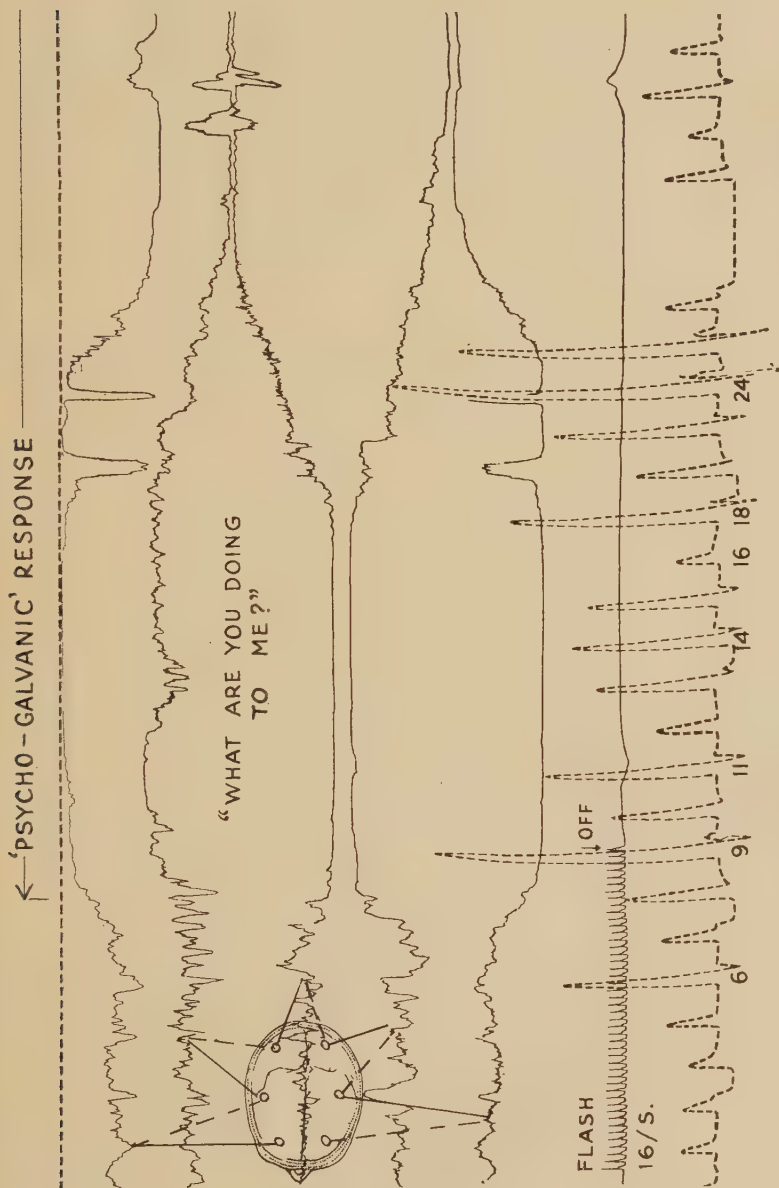


FIG. 1.—EEG and PGR (slow deflections) from epileptic patient during and after brief exposure to flicker at 16 f/s. Note complex analysis with components unrelated to stimulus frequency. After several such preliminary exposures, typical wave-and-spike patterns were evoked instead of the affective response.

the psychoneurotic category, it was repugnant to regard her as an experimental animal. However, a sufficient number of records has been collected and analysed to define the nature of the anterior cortical discharge in this

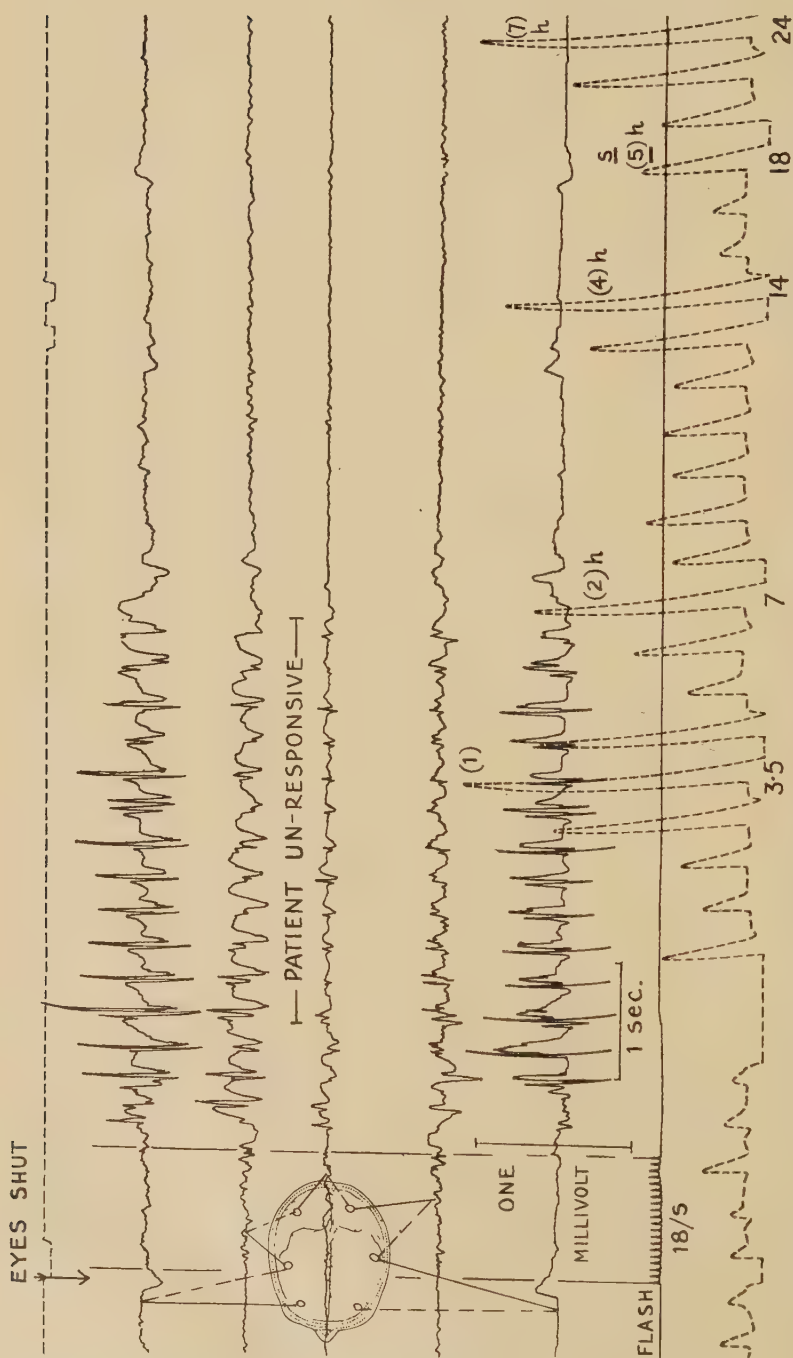


FIG. 2.—Typical wave-and-spike pattern evoked by flicker, *only* when at 18 f/s and synchronized with closing the eyes. Note components in analysis as near-harmonics of 3.5, including 18, although the seizure pattern and analysis begin only after the end of the stimulation. This record is representative of ten such activations obtained in the patient within a few minutes. There were no abnormalities in the resting or hyperphoea records.

person. The first striking feature of this is that it has its own frequency, which falls as its amplitude rises, whatever the frequency of the stimulus between the limits already given—8/12 f/s. The second feature is that the discharge dies away slowly when the stimulus is interrupted, remaining visible at diminishing amplitude for from 5–10 seconds. The records are sufficiently similar to permit rough mathematical treatment of the oscillation and, technicalities omitted, this suggests that at least two major mechanisms are operative, one of frequency selection, the other of release; the only mechanical analogy I can call to mind is an alarm clock without a main spring; but a fifth second escapement which is arranged to go off every second. Since this patient was

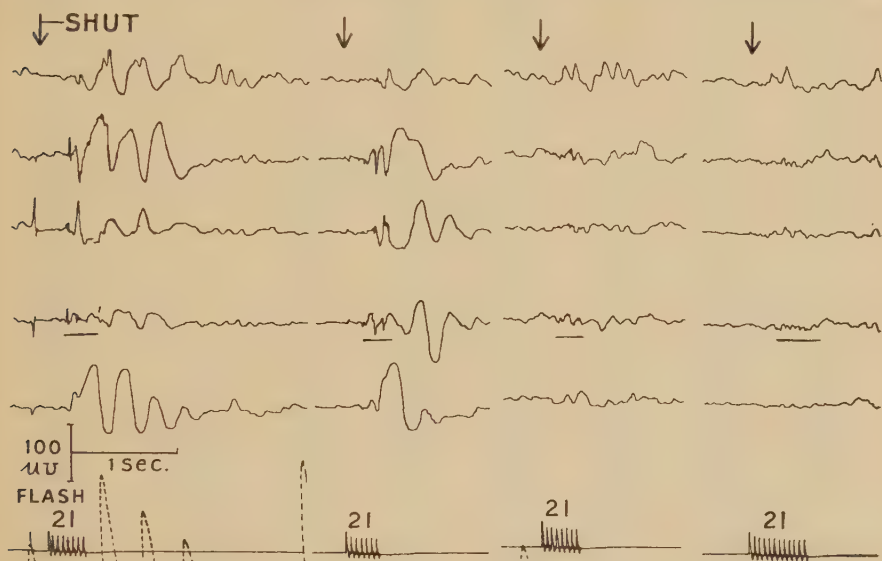


FIG. 3.—Activation of a slow mechanism by brief exposure to flicker *only* as the eyes were shut. The four exposures were made within 20 seconds and show a progressive reduction in amplitude of the secondary discharges, only the elementary ones being visible in the fourth exposure.

first seen we have observed several more without hint of epilepsy who have responded paroxysmally to photic stimulation; three give responses similar to that described, one had a typical *grand mal* seizure, others have had minor attacks of various sorts. One additional feature which has appeared is that, as in the case of the normal psychic activation, the response is sensitive to mood and atmosphere. One patient who gave frontal spikes and jerks as an out-patient had only headache and frustration as a history; after a day as an in-patient in a friendly and reassuring environment her record showed no sign of the previous anomaly; her gain was our loss. Another patient who had a history of violent behaviour, also showed spikes and jerks under flicker, but he objected to being thrown around, and tensed his muscles, which were well developed, and the cerebral and peripheral discharges were immediately abolished. The importance of a neuromuscular retroaction or feedback in these states is quite great and one should recall the experiments of Gellhorn

which indicated a similar process in chemically induced convulsions in animals. There seems no doubt, therefore, that an epileptic type of discharge can be evoked in people who have never had a seizure, by physiological stimulation

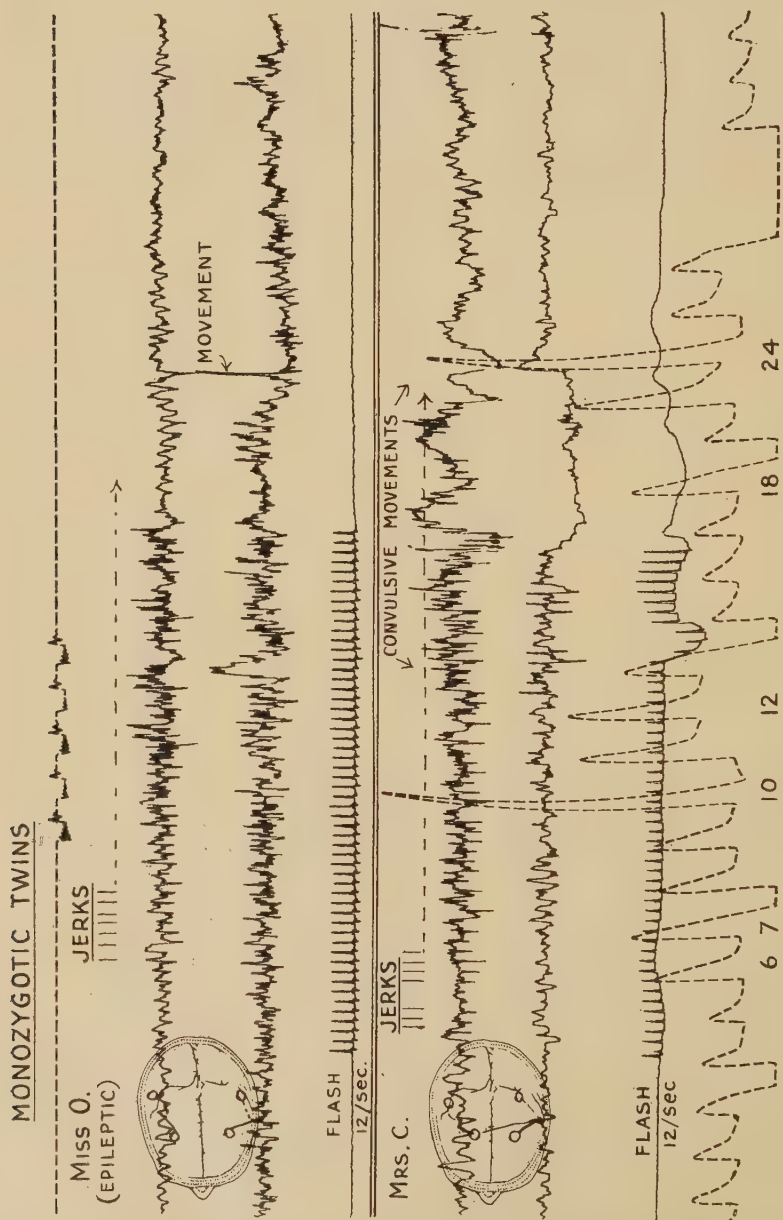


Fig. 4.—Records obtained simultaneously from two identical twins, showing the similarity of response to flicker—frontal spikes and myoclonic jerks.

in the right mode and rhythm. The only other physiological anomaly which seems to be commonly associated with this effect in sensitive subjects is some sort of hypothalamic disorder, evidenced by disturbance of sleep, water metabolism, temperature regulation, hypophyseal function and the like. A quan-

tative assessment of this correlation would be valuable, but has not so far been within our capacity—one insuperable difficulty is that psychological treatment has important effects, and since this cannot in human charity be

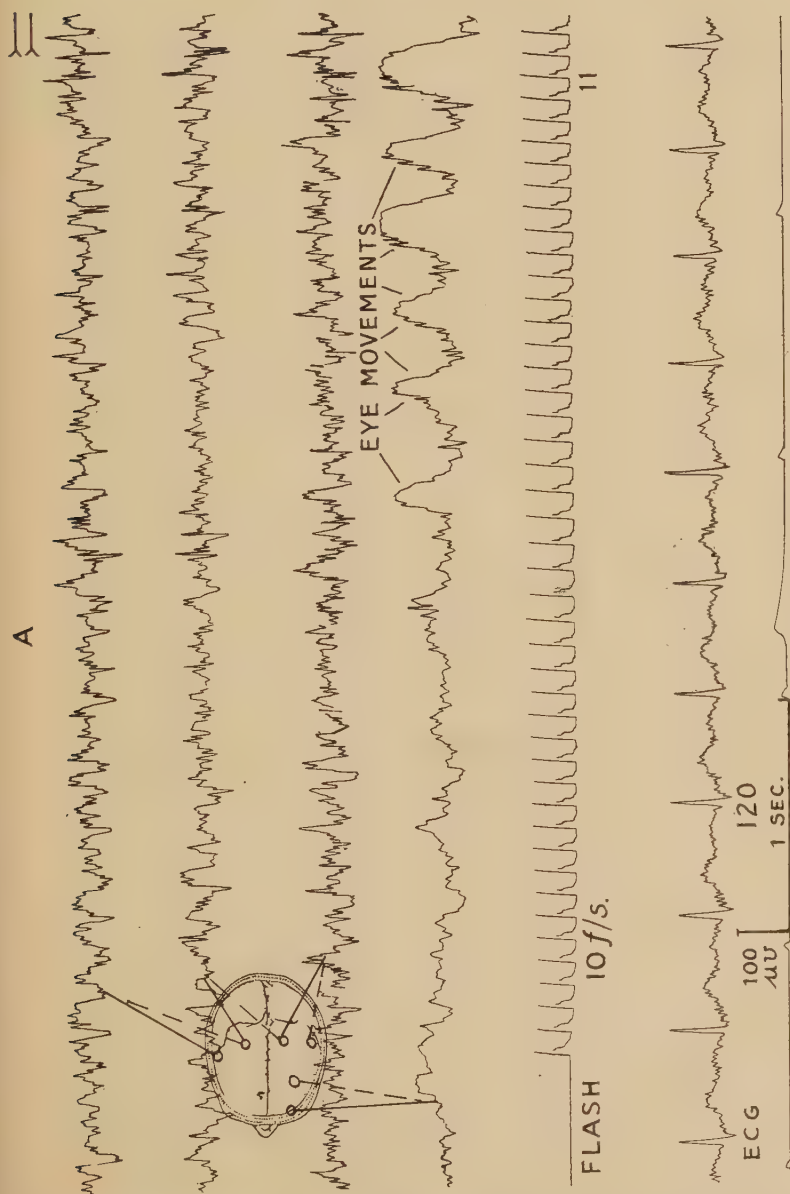


FIG. 5A.—Evocation of frontal spikes and myoclonic jerks in a *non*-epileptic patient. A. The start of the exposure, showing the first few frontal spikes. B. Continued from A, the muscular movements begin about 6 seconds after the start of stimulation. The flash rate is reduced to about 8 f/s. C. The discharge culminates in very large spikes and violent jerks, the frequency falling as the amplitude rises. The discharge persists for several seconds after the stimulus ends, and rises again in frequency as its amplitude falls. The pulse accelerates from 120 to 145 per min.

withheld, the conditions are never constant but, indeed, are deliberately changed as rapidly as possible.

Patients with a combination of epilepsy and psychic disturbance provide remarkable opportunities for physiological study, though as I shall explain later, the physiologist finds himself being drawn inexorably into the experi-

mental circuit and usually in an undignified position. One patient with a history of occasional attacks and considerable psychological instability and eccentricity, responded at 6 f/s or multiples of this with piercing screams and

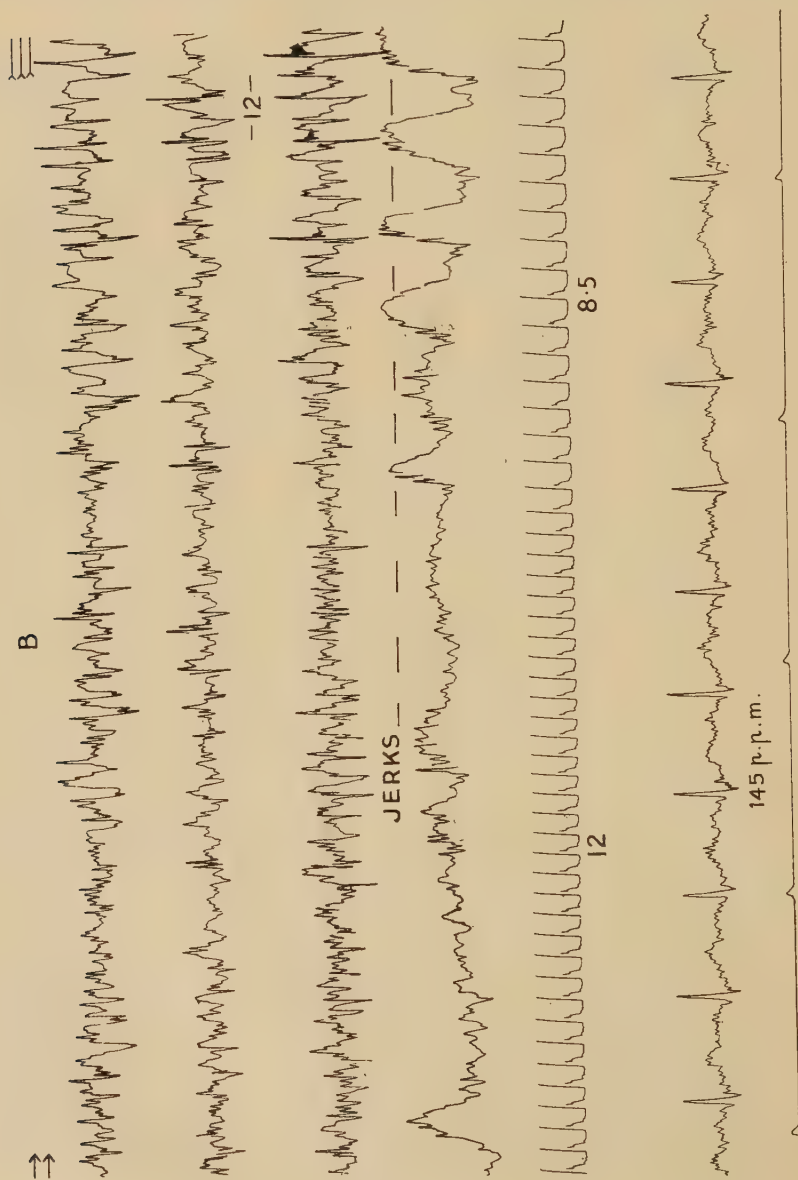


FIG. 5B.

heartrending sobs, exclaiming between outbursts that it was "perfectly all right" and she didn't mind at all really! (Fig. 6). This could have been an hysterical attack of a particularly novelettish type, but the record showed abrupt and ample discharges in both temporal lobes at 6 c/s which persisted for some time after the stimulus was terminated and the tears were stanchd.

Psychological aggravation was particularly effective in this case, and so also was assuagement, for a few kind words and interest in ordinary things before the examination would greatly reduce the response ; while it was of the order

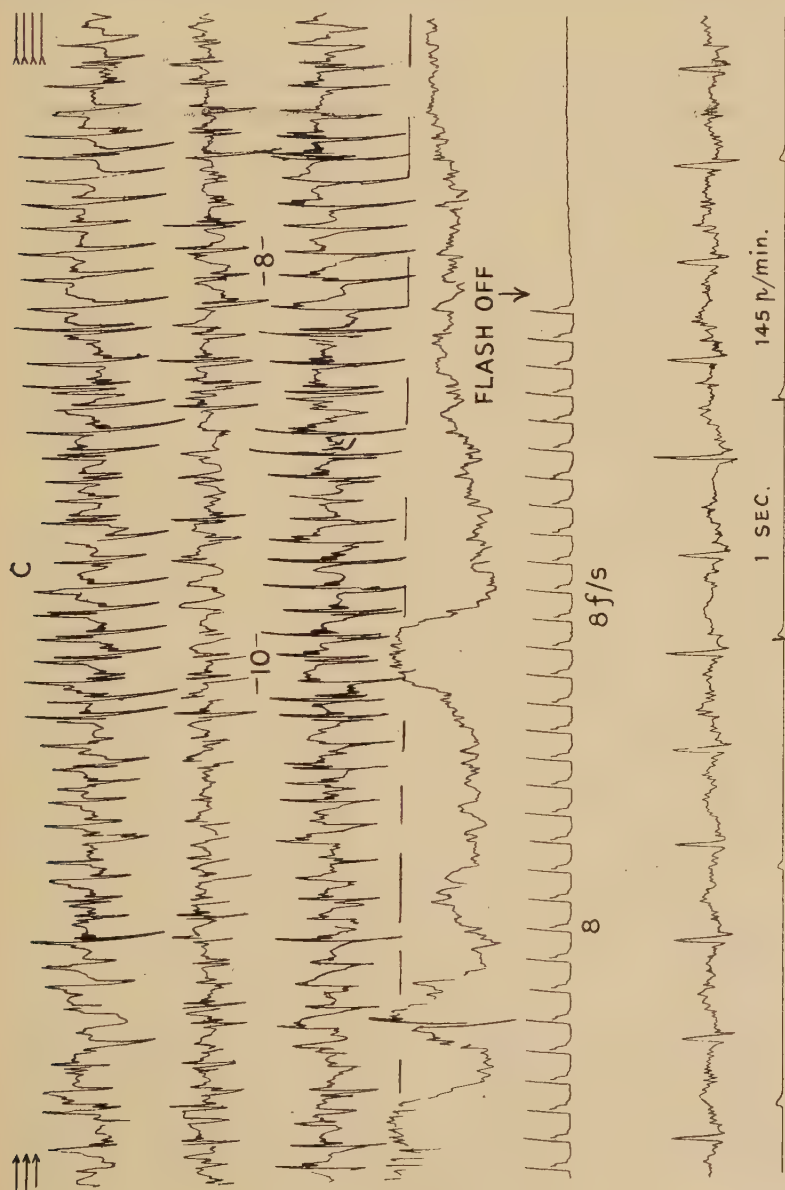


FIG. 5c.

of 200/uV when the examination was done by a woman, it was about 100/uV when done by a man, and zero when there were two men present after a few minutes of conversation. This variation was quantitatively repeatable. This patient was able to paint vivid pictures of her sensations during the experiments; those during the early stage of violent response were sombre and

asymmetrical; during an experiment, when she did not break down, they were similar to the illusion seen by most people. On a third occasion, when she had been psychologically aggravated and then mollified they were intermediate

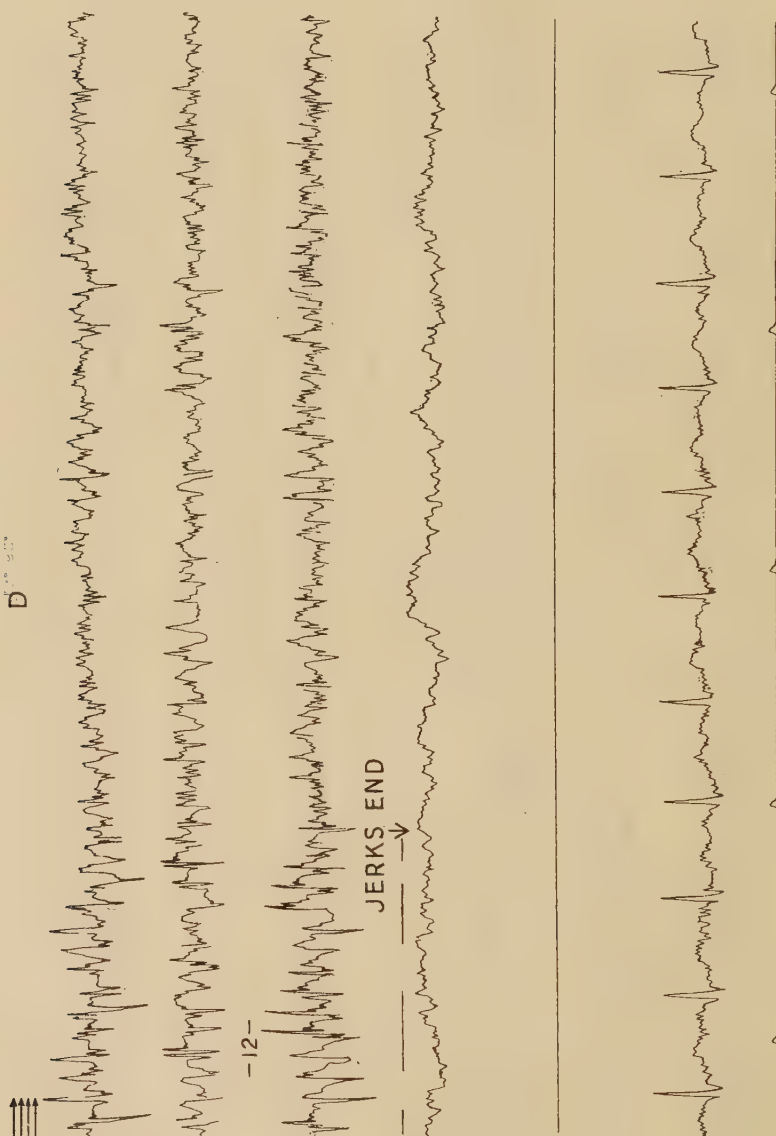


FIG. 5D.

but particularly dynamic and colourful. (I am not presenting these as physiological data, but we may have to accept such products as having the same validity as our electrical records—and possibly more immediate significance.) In this case the epileptic aspect of the activation was proved by the fact that, whenever the exposure was continued in spite of the patient's outcries, for

more than half a minute or so, a characteristic generalized *grand mal* convulsion developed, heralded by a spread of the temporal discharge to the central and frontal regions. To the further psychiatric aspects I will return later.

You will have noticed, as we did, that by far the commonest of the secondary discharge areas are the temporal lobes, and of the frequencies those in what I have called the theta band are the favourite. It is *not* perplexing that the temporal lobe should be particularly accessible from the visual areas, since the tertiary and quaternary association areas are midway between the two and the rhythmic stimuli would be expected to break through the scanning mechanisms which connect these regions in a particularly forcible way. But what does intrigue us is the relation between the theta rhythms evoked in these regions by rhythmic stimuli and those which appear spontaneously in children or psychopathic adults, cases with deep lesions and so forth.

In children the theta components are exquisitely responsive to emotional stimuli, with the aid of which two or three components in this band can be recognized. With advancing maturity the effect subsides and in the normal adult, only the most disagreeable stimuli can produce any effect of this sort. In fact few experimenters have tried seriously to evoke theta activity in normal adults because to be effective the stimulus must be authentic and thoroughly offensive—one's enemies are not likely to deliver themselves into one's hands, of strangers one is unlikely to know anything sufficiently telling, and one's friends one cannot by definition offend. We searched for some time for a stimulus which would have the desired effect, and while trying a pleasant instead of an unpleasant one found an answer. The stimulus was actually intended to be gentle tickling of the face, but deteriorated into a stroking movement, which the subject found agreeable and soothing. There was no change in either primary record or analysis during stimulation, but when the stroking was *stopped* the amplitude of the theta component in the temporal analysis rose to about eight times its original value. Though the effect could be repeated as often as desired, I was not quite satisfied until I had actually seen the rhythm in the primary trace from the temporal lobes. Only a few subjects show the change as above the level of random disturbance in the primary trace, but in some it is as clear as the start of the alpha rhythm when the eyes are closed, the difference being that the duration of the discharge is usually only about 10 seconds (Fig. 7). The temporo-parietal location is easily verified either with the analyser or by the direct method, and further spatial analysis shows that in most subjects the discharge is from a region equivalent to a slice about 2 cm. from front to back and 5 cm. high from the temporal to the parietal lobes, the equivalent generator being orientated transversely and extending obliquely deep into the centre of the head. I think it is rather intriguing that we should have evidence of some mechanism that responds not to pain but to minus-pleasure—a sort of affective off-effect with a long latency—the implication seems to be that the mechanism made visible as theta activity is seeking for pleasure as the alpha rhythm may be said to seek for pattern.

But there seems to be more in these records than empirical support for the ancient scholastic doctrine that good is bad by privation. If we look at them

closely we find a quite startling uniformity about each experiment. The examples I have selected are two from dozens, and I have not, unfortunately,

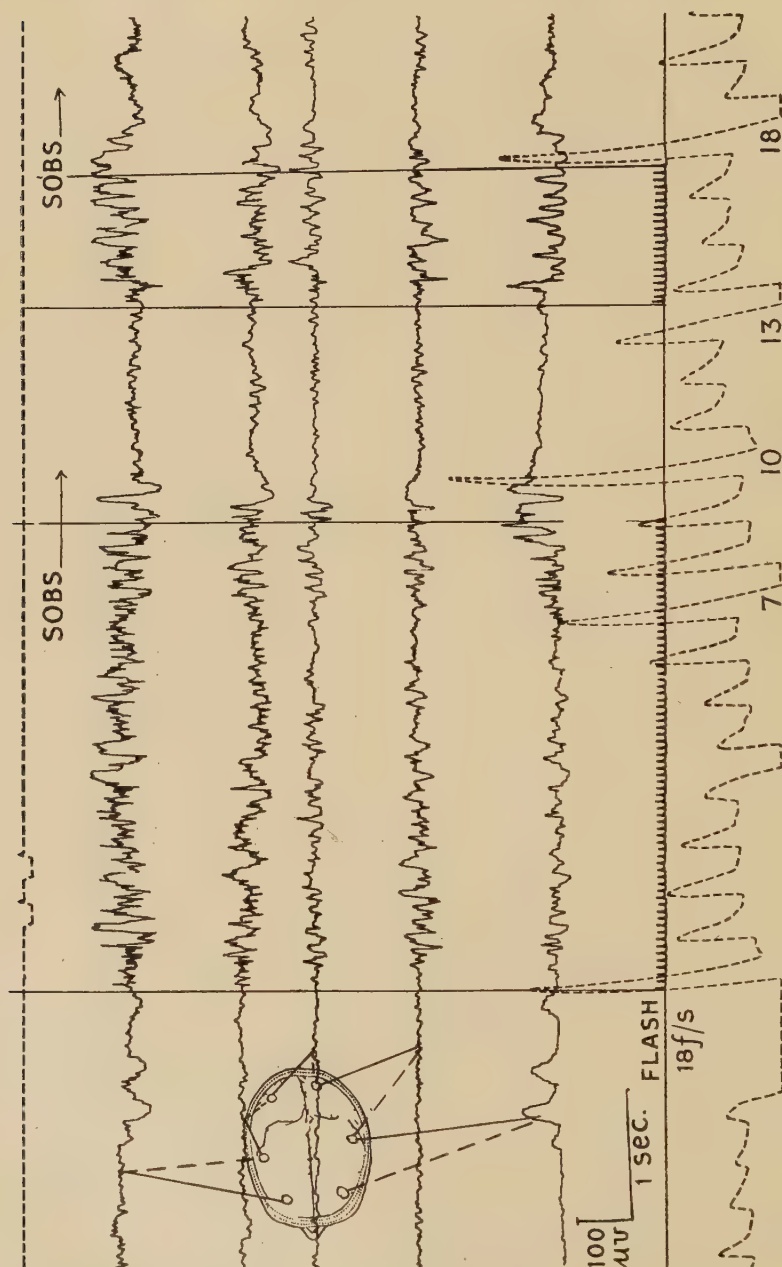


FIG. 6A.

had available during the last few weeks facilities for constructing the composite of a large number in a form fit for exhibition, but even a cursory inspection suggests that not only does the crescendo of temporal theta begin and end at

exactly the same instant, but many of the details of the discharge recur in both these records, and what is more, they recur in nearly all of those taken within a few hours. Now, the only other condition in which a complex pattern

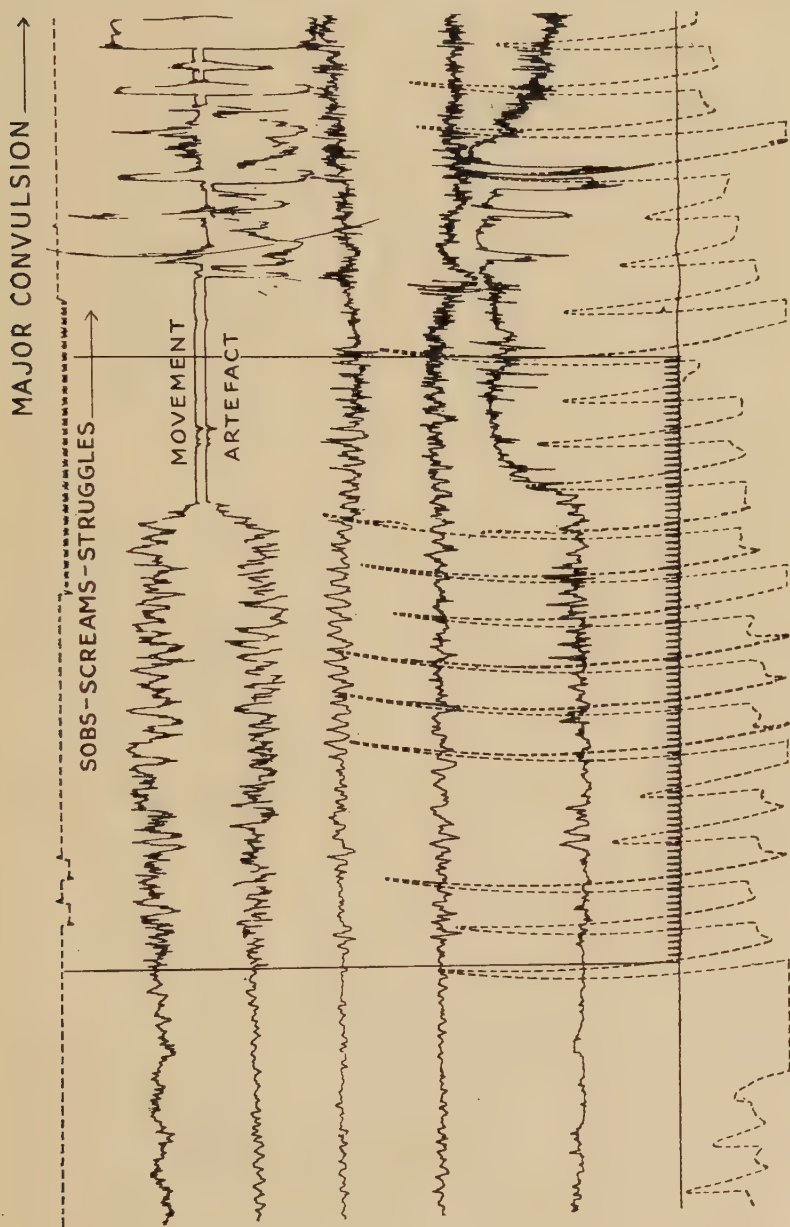


FIG. 6B.—Evocation of emotional outbursts in epileptic by short exposures to flicker at 18 f/s leading up to a generalized convulsion with longer exposures.

repeats with obvious regularity is the wave-and-spike of *petit mal*—but here there is absolutely no question of a seizure, nor, of course, does the pattern bear any resemblance to a wave and spike. Further, the pattern is far more complex and repeats not cyclically but as a whole over a period of several

seconds at least. I find it difficult to avoid the implication that in such records we have before us an electrical transcript of an elaborate and purposeful *thought process*, involving the systematic rhythmic excitation and inhibition

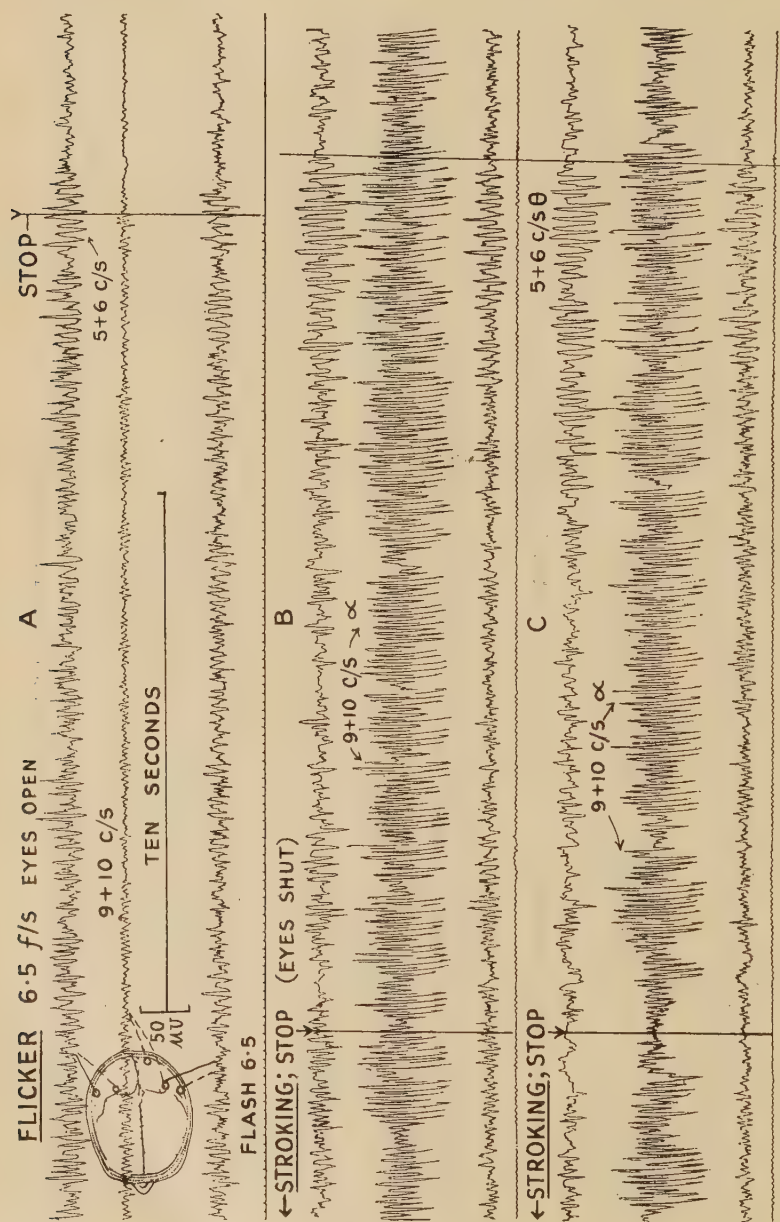


FIG. 7.—A. Evocation of temporo-parietal theta rhythm in psychoneurotic by flicker at 6.5 f/s. Note location, complexity and after-discharge of the response. B. Evocation of similar activity in same subject by termination of agreeable stimulation. Note slow crescendo of theta rhythm, its independence of occipital alpha rhythm and sudden termination 17 seconds after the end of the stimulation. C. Record from same subject taken a few minutes later. Note the similarity in details of the response.

of great numbers of cerebral elements in a manner which is sufficiently stereotyped for us to recognize, as it were, a single character of the great cipher. If you glance again at the record showing evocation of theta activity in the same subject by flicker you will see that although the mean frequencies are the same,

the pattern is different ; there is a short after-discharge and the response frequency is not exactly that of the stimulus, so we can consider the response as an imminent mechanism, but there is rarely—except in epilepsy and those non-epileptics who develop paroxysms under flicker—anything like the degree of superimposability in evoked discharges that there is in those which develop gradually, either spontaneously or under the action of less potent stimuli.

You will appreciate that to recognize a repeating pattern against a random background is excessively difficult unless there is some fiduciary mark on which a number of samples can be aligned. Whenever there is a stimulus or a recognizable action, superimposition can be attempted. In this way, Bates has shown that if a spontaneous voluntary movement is taken as fiduciary mark, then for half a second or so *before* the movement the EEG pattern takes on a standard form ; some component of the alpha rhythm seems to bear a very close phase relation to the release of centrifugal signals. By another method Richter and Kibbler have collected evidence that the moment of initiation of eye movements and other actions is similarly related to the phase of an alpha rhythm. Now you will recall that in our behaving toy we had to synchronize the effector “servo” with the receptor scanner to reduce wander and backlash, and predicted that some such device must be present in a well-designed nervous system—it seems as though this necessity has indeed not been overlooked in the central nervous system. In the case of the repetitive patterns in the theta band, however, it is not so clear that any specific effector system is being gated or synchronized, but there is physiological evidence of autonomic activity in various modes and the major component appears to be a psychic one. In the experiments with theta rhythm the commonest feeling is one of frustration, sometimes of anger, and I feel reminded of the suggestion of Craik—which is not, of course, very different from the notions of the ancients—that the function of the mind is to construct and contain working physiological models of environmental problems. It is just conceivable that some of these records may be profiles of working models of action which the subject does not quite permit himself to use. In many subjects a state of extreme tension and self control reduces the regularity of the evoked theta assemblies, while in less trammelled moments they appear more often and in more recognizable patterns, as they do in some people in that blissful drowsiness before sleep when the desirable and the possible seem to coincide without call to action.

I am increasingly disposed to use the word “temper” to describe cerebral states, as it contains the notion of time and tuning—certainly the appearance of a theta rhythm is usually a good sign of a bad temper.

There is another function which the normal rhythms may have—or perhaps one should consider this as another aspect merely of their general function—that of storage. Referring again to our model, we found it convenient to endow the machine with a short-term memory in the form of an oscillation, engendered by contact with awkward obstacles ; now an oscillation is about the most compact storage register one can imagine, since it is a process, not an object at all. Furthermore, it can be arranged to die away at almost any desired rate, and, if required, to call forth or be evoked by any similar process which has a nearby or related frequency. This provides not merely storage, but

forgetting, recall by similarity, and the synthesis of "novel memories" by the superimposition of many components. It is interesting to note that if such a mechanism has the property of rapid growth, it will also tend to decay rapidly and will be less selective, in the sense that it will respond to a wider range of signal frequencies. As you have already seen, many of the evoked rhythms which we have been studying undoubtedly have some of these physical properties: their participation in at least the cruder sorts of remembering is strongly suggested by the ease with which they can be conditioned and, of course, by my earlier demonstration that rhythmic excitation at certain frequencies evokes apparently irrelevant sensations and actions which are, all the same, wonderfully consistent in any individual, but vary between individuals. Until there is very strong evidence to the contrary I suggest that rhythmic oscillation between cerebral elements as a physical basis for short-term memory is a fertile working hypothesis. Whether an entirely different mechanism must be responsible for long-term memory is another story; the vulnerability and evanescence of recent memory and of dreams contrast so much with the toughness and rigidity of long-acquired behaviour that a difference of quality rather than of quantity is indicated.

There is a growing mass of evidence that the persistence of evoked rhythms may be much longer even than that shown in the records you have seen. Significantly, the persistence is usually longest in regions remote from the primary sensory areas. In many epileptics, for example, exposure to any single frequency has only a slight effect upon the record, but if after exposure to one frequency, another related one is used, a seizure pattern will be evoked, and the preconditioning effect may last for several minutes. More striking still, Thomas has found that in some psychotic patients the response to a given flicker frequency may persist for more than ten seconds, even when the rate of stimulation is changed—here, again, the effect is often seen in the anterior frontal region.

Which, if any, of the spontaneous rhythms have a storage function cannot, I fear, yet be decided positively. The isolation of a frontal rhythm at about 8 c/s in some persons—the "kappa rhythm"—which is augmented during mental effort is suggestive, and even in apparently quite irregular records from the temporal and frontal regions analysis shows many quite rhythmic though excessively minute components in almost all the frequency bands from 4 to over 50 c/s. Many of these are extra-cerebral in origin, and I cannot feel confident about their significance until we have been able to identify them with specific states. There is a possibility that we are looking at these intimate details of cerebral economy in entirely the wrong way, rather as though one tried to appreciate a television signal by listening to it on a loudspeaker. We must cast about for the co-ordinate system which brings the picture to life and remember that though we have to communicate with one another by a succession of signals strung out in time, the thread may be drawn from a patterned web and not from a spool as our recording paper is. What an inspired image was Sherrington's—"an enchanted loom."

My thread at least is coming to end—a loose one I fear—but two tangles remain to be at least fingered. There is one group of rhythms—if it is a group

—which I have scarcely mentioned: those slow swells and surges which rock the infant, rack the adult brain. These seem at first sight to be designed solely for the gratification of the electroencephalographer, since their correlation with function seems a purely inverse one. Ten years ago, while I was trying to imagine some physiological justification for such electrical largesse, it occurred to me that we have no logical right to assume which is cause and which effect in this matter; from the point of view of the brain itself an electric field of current is antecedent to function. Further, considering that the brain lacks the three defences against injury which most other parts of the body possess—pain, lymphatic drainage and repair—it would be reasonable to find in it some special device which would immobilize and protect a threatened region and also prevent it from deluging the healthy survivors with futile and confusing signals ensuring what engineers call “failure to safety.” There is other evidence, too, the wide prevalence of slow rhythms in healthy states of inaction, infancy and deep sleep, the inhibitory effect of artificial slowly changing currents, and perhaps most challenging, the strange absence of peripheral accompaniments of the enormous spike in the wave and spike of *petit mal*. In one of the records you have just seen (Fig. 2) there was a series of spikes in the motor region equivalent to one millivolt, as seen with scalp leads. Why did this huge voltage have no excitatory action whatever upon the rest of the body while a considerably smaller one in other cases with no slow waves (Figs. 4 and 5) threw the whole musculature into convulsive movement? I feel that if all the data had been presented to us at once—subjective, neurological and electrical—we should assume quite naturally that the generation of slow electrical oscillation is the mechanism whereby the organism is protected from the consequences of cerebral immaturity, exhaustion, damage and excessive discharge. That the mechanism is not always successful is no evidence against it, for, indeed, we must recognize that in the end, all individual physiological battles are lost.

Before concluding I feel bound to mention at least the basic problem of how the structure of these rhythms we have been discussing is related to the bricks of anatomy and electrophysiology, the nerve-cell and its action potential. Their rhythmicity I think we can safely assume to be evidence of retroaction or feedback of some sort somewhere. One question is, can such activity be due to what Bremer has called the “autorhythmicity” of cell-bodies and their processes, in which case the feedback would be in the cell itself, or must we postulate a true circuit, involving numbers of cell units in which the signal traverses in effect a circular path? Completely isolated cortex is not usually spontaneously active, as Burns has shown, but in certain excitatory conditions it may become so—as indeed an axone may. Conduction by summated field effects without synaptic assistance or axonic continuity again is unusual in peripheral or spinal preparations, but can occur; it does not assist the paraplegic, though it may complicate the recovery in the leucotomized patient. It would be absolutely astounding if in a structure such as the brain a signal never returned to its origin in such a way as to maintain an oscillatory discharge, quite apart from the specific evidence of interdependence between cerebral regions which has been collected from animal experiments and from

man. To me the evidence on both sides seems completely convincing and, the history of science being full of true assertions and false denials, I would judge both sides victor—but to discriminate between the two effects in any particular case is a rare puzzle for the experimenter.

As to whether the activity we see in our human records is the statistical view of briefly discharging neurones and axones, we can only say that there is no evidence that it is not, and be thankful that some part of the pattern of these discharges is visible to us. In the sort of experiments I have been describing, the activity of single units seems of no greater relevance than the behaviour of a single ion in a chemical reaction; the removal or destruction of great numbers of units seems to have a negligible effect upon function. The study of brain function can only be statistical in this sense because the brain can only function statistically in relation to the environment.

I shall not venture further into the philosophical levels which were explored so expertly by my leader and colleague, Professor Golla, in the eighteenth Maudsley Lecture which he delivered twelve years ago. This lecture was a milestone in our progress and I think we can legitimately look back upon it with some sense of having travelled. I think he would agree with me that we need not assert with such finality that "The continuity of mental processes does not allow of their representation as states of mind, their interrelatedness does not allow of their separation in terms of psychological atomism. The intuitive and instinctive basis of conduct does not permit of analytical expression." This dilemma, how to study a continuous process in terms of discrete states is still with us, but I do not think we need maintain our reasonable scepticism in quite so absolute a form.

Next, one of my favourite quotations from the Introduction by Roger Cotes to the first English translation of Newton's *Principia* in 1729: "Some I know disapprove this conclusion and mutter something about occult qualities. They continually are cavilling with us, that gravity is an occult property: and occult causes are to be quite banished from philosophy. . . . These rather have recourse to occult causes; who set imaginary vortices, of a matter entirely fictitious and imperceptible by our senses, to direct those motions.

"Some there are who dislike this celestial physics because it contradicts the opinions of Des Cartes; . . . but let them act fairly, and not deny the same liberty to us which they demand for themselves . . . let us have the liberty to follow causes proved by phenomena, rather than causes only imagined and not yet proved. The business of true philosophy is to devise the natures of things from causes truly existent and to enquire after those laws on which the Great Creator actually chose to found this most beautiful Frame of the World; not those by which He might have done the same had He so pleased. . . . The same motion of the hour-hand of a clock may be occasioned either by a weight hung, or a spring shut up within. But if a certain clock should be really moved with a weight, we should laugh at a man that would suppose it moved by a spring, and from that principle suddenly taken up without further examination should go about to explain the motion of the index; for certainly the way he ought to have taken should have been actually

to have looked into the inward parts of the machine that he might find the true principle of the proposed motion. The like judgment ought to be made of those philosophers who will have the heavens filled with a most subtle matter which is perpetually carried round in vortices."

Well, the relation of vortices to mental states is almost as inaccessible to us as the heavens were to Newton, but I think he would agree that if one cannot take a machine to pieces to see whether its rhythm is from a spring or a weight, one might reasonably start by shaking it and even perhaps end by turning it upside down.

THE SOMATIC MANIFESTATIONS OF SCHIZOPHRENIA.* A CLINICAL STUDY OF THEIR SIGNIFICANCE.

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INTRODUCTION.

THERE is still no agreement on the aetiology of schizophrenia, or general acceptance of its definition as a "functional psychosis." There is agreement only on the complexity of the problem presented by an illness which involves every aspect of the personality, and is precipitated by a multiplicity of internal and external causes. This complexity suggests that an approach from many angles, clinical, genetic, sociological, statistical, or even a more remote biological or physiological approach may yield some information of value.

These considerations have prompted a reinvestigation and a discussion of some of the somatic manifestations of schizophrenia. The observations were carried out in the ward and at the bedside, and while they lack the precision of laboratory experiment they have the advantage of continuous clinical contact with the material studied. They were collected during four years spent in close proximity to the psychotic population of a large County Mental Hospital.

The cutaneous vascular disturbances of schizophrenic patients were studied in the first instance as they present objective signs which are unmistakable and are easily observed. This choice of subject was also suggested by disagreement expressed in the writings of various investigators on the significance of these disturbances in relation to the mental illness. It was only by repeating and confirming the work of others, who frequently worked under better experimental conditions, that any opinion could be formed on the nature of these vascular disturbances and of the reason for their differing interpretations. The cause for this discrepancy appears to lie in the isolation of an experimental observation from its physiological and psychological setting. As an example, a compensatory reaction only appears as such if the total situation is taken into account; it is otherwise indistinguishable from a primary causative event and acquires a different physiological or pathological significance.

In the following study this consideration has always been kept in mind and an effort has been made to present the facts in relation to what is known of the total setting.

The report of the clinical observations on cyanotic, vascular and thermal derangements of mental patients is presented separately, followed by a review of the relevant literature. More scattered observations, which were suggested

* An M.D. (Psychological Medicine) thesis, awarded the Gold Medal of London University. Reference is made in this text to a few additional publications which became available after the thesis had been completed for presentation.

by the initial study, are reported in conjunction with a survey of more extensive work undertaken by others in these various fields of psychosomatic derangement. The subject matter is divided by arranging it under headings related to functional levels, i.e. peripheral, glandular, central nervous system and psychological. In conclusion, the material is gathered together in an attempt to interpret the nature of schizophrenic illness in the light of this study, and some conclusions are tentatively put forward.

The designation "schizophrenia" is employed throughout in the sense in which it is used at the hospital where these observations were made. It represents a consensus of local opinion, rather than an entity defined by a particular school of thought, each patient having been seen by several medical officers from the time of his admission from the clinic, or directly to the hospital wards as a voluntary or certified psychotic, up to the time of his discharge, or transfer to one of the chronic wards. Diagnosis and "labelling" are briefly discussed later, but it may be said now that a primary diagnosis of schizophrenia on admission was seldom reversed in the course of years, whereas shifting from one schizophrenic sub-group to another was a common occurrence. Exceptions to this rule are the occasional renaming of chronic mania, and the more frequent renaming of a confusional psychosis, as schizophrenia.

The only two subdivisions which emerged clearly, when the schizophrenic population was surveyed as a whole, were the catatonic and paranoid sub-groups, the latter including a small number of cases labelled paraphrenia or paranoia. These two syndromes were, however, frequently combined, or occurred successively in the same patient. The hebephrenic group was ill-defined clinically from mental deficiency and was complicated by cases described as "schizophrenic illness occurring in a mental defective," or "schizophrenia following traumatic or encephalitic deterioration." The isolation of this group was therefore not found possible and doubtful cases are considered, for the purpose of this study, to be suffering from mental deficiency.

A STUDY OF CYANOSIS AND VASCULAR RESPONSES IN PSYCHOTICS.

Cyanosis and other vascular disturbances in psychotic patients have been noted by many observers. Cornell (1) considered the cyanotic hand of dementia praecox to be pathognomonic of this illness. Mapother (2) described cyanosis and oedema in advanced cases of dementia praecox and believed it to be often, but not always, referable to posture and immobility; Bleuler (3) remarked that without comprehensible reason livor and cyanosis were frequently present and in rare high-grade cases a blue-black discoloration of the hands and feet could be observed.

During routine medical examination of the patients of a County Mental Hospital cyanosis of the extremities was often observed in chronic female psychotics, particularly in those suffering from a schizophrenic illness; it was less frequently seen and was usually transient and much less severe in both male and female patients suffering from an early schizophrenic illness, and was rare in chronic male psychotics. These preliminary observations suggested that examination of a larger number of psychotic patients of both

sexes, who resided in this hospital, would be of interest and that it might elucidate the causes which underlie peripheral vascular disturbances in these patients.

Seven hundred patients, 300 men and 400 women, were observed under various environmental conditions: three hundred male and 220 female patients were examined at ordinary ward temperature during the summer months, and 240 female patients were examined at a higher indoor temperature. Later, observations which extended over three years were made on smaller groups of patients on the lines suggested by the preliminary investigation.

Criteria of Cyanosis.

The term *mild cyanosis* is used to indicate a change of skin colour which is similar to that seen on the hands and feet of normal persons after moderate chilling, but which is generally absent in persons observed at room temperature during the summer months. Mild cyanotic discoloration corresponds to tints VII–X of Sir Thomas Lewis' scale (4). When seen on the feet and hands of psychotic patients it usually extended above the ankle, or higher up on the leg, fading below the knee; the thighs were rarely involved. When the hands were cyanosed the colour usually faded above the wrist. Occasionally the skin of the face and other parts of the body were also involved. Cyanosis was as a rule evenly distributed over the affected parts; the colour was light and varied from heliotrope to a greyish blue.

The term *severe cyanosis* is used to denote more definitely blue discoloration of the skin and a greater depth of colour. The distribution of deep cyanotic discoloration was uneven, the skin was frequently mottled and blotchy, the darkest areas being usually situated on the lower and outer aspects of the legs and feet. Small, bright red patches of skin were often present on the toes and legs of patients suffering from severe cyanosis. The worst cases presented a striking appearance, their feet, and less frequently their hands, being blue-black, or a dark plum colour which corresponded to Lewis' scale tints XI–XV. The colour of deeply cyanosed feet shaded-off above the ankles; the hands were rarely as deeply discoloured as the feet, but in a few patients cyanosis of the hands was also extreme (tint XV of Lewis' scale); the face and body-wall were never very dark. Occasionally only one or two toes showed deep cyanosis. In patients who suffered from severely cyanosed feet and legs, the skin below the knee was dry, scaly and inelastic; superficial scars on the toes and heels indicated the site of healed chilblains and pressure sores. In a few cases the tips of one or more toes were missing, and the nails were atrophic, deformed or absent. The dorsum of the foot was frequently puffy where it was unsupported by indoor shoes. There was occasionally a little pitting on pressure, but less than one would have been led to expect from the degree of swelling; the ankles were occasionally swollen, but pitting oedema of the upper half of the legs was never observed.

Other Changes Noted at Examination.

Pigmentation, light brown in colour, punctate, patchy or evenly distributed, was seen on the back, chest and abdomen of some female patients, mainly,

but not exclusively, in patients who also showed peripheral cyanosis. Pigmentation was never observed in male psychotics. In female patients, dark pigmentation of the nipple and areola was not rare and was sometimes striking, being darker than that frequently associated with pregnancy. The distribution of the areas of cyanosis and pigmentation did not correspond, and as these conditions also occurred separately, they may be unrelated. Pigmentation of the mucous membranes was never observed.

Sweating.—The palms of the hands of patients who showed cyanosis were dry in some cases, moist in others, and in a few cases sweating was excessive. No relation of sweating to the degree or to the presence of cyanosis was evident.

*Examination of 520 Psychotics (300 Males and 220 Females)
at Room Temperature 62–65° F. (16·7–18·3° C.).*

(See Tables I and II.)

These patients were unselected, except for the exclusion of senile and sick-bay patients and of those believed to be suffering from an organic psychosis. Approximately 5 per cent. of the female patients and 2 per cent. of the male patients were early cases of mental illness, of less than 18 months' duration, the others were chronic psychotic cases. The male group consisted of all available patients between the ages of 17 and 65 who were sufficiently co-operative. The female patients were drawn from wards situated near the examination rooms, an admission ward, a ward for socialized patients and one for difficult or mentally deficient patients. They were aged 15 to 65 years; just over one half of all these patients, both male and female were between the ages of 25 and 50, rather less than one quarter were under 25 and just over one quarter were over 50 years of age. Approximately one third of both the male and female patients were employed in wards, kitchens, laundry and occupational therapy centres; one third were occasionally employed, the remaining third were uninterested or deteriorated patients who were unemployable except at a few simple tasks such as wool picking and polishing, done under supervision.

Conditions of Observation and Clinical Findings.

These patients were examined during the summer months in moderately warm weather, with indoor temperatures ranging between 62° and 65° F. (16·7–18·3° C.). Wearing their indoor garments, 10 to 15 patients rested for half an hour on chairs arranged in a semicircle. Room temperatures were taken with a thermometer suspended in the centre; draughts were excluded by closing doors and windows. After these patients had rested, their arms and legs were bared, and the presence, or absence, of cyanosis was noted; they were then undressed to see whether cyanosis or pigmentation of the body was present. These observations are summarized in Table I. (In this and in other tables the term "cyanosis of the feet" includes cases in which a few inches of skin above the ankle is also involved. Extension of cyanosis to the knees was less frequently found and is recorded separately.)

TABLE I.—*Cyanosis and Pigmentation.**Observations at room temperature 62–65° F. on 300 male and 220 female psychotics.*

Room temp. 62–65° F. (16·7–18·3° C.).	300 Male psychotics.		220 Female psychotics.	
	Number.	Per cent.	Number.	Per cent.
Cyanosis of extremities	16	5·3	95	43·2
" of feet.—Mild	10	3·3	54	24·5
" " Severe	1	0·3	35 ⁴	15·9
" of hands.—Mild	12 ³	4	29 ⁵	13·2
" " Severe	2	0·6	4 ⁶	1·8
" of face ¹	1	0·3	24 ⁷	10·9
" below knees	1	0·3	28	12·7
" of whole leg	..	..	2	0·9
" of forearms	..	..	4	1·8
" of breast ¹	..	..	6	2·7
" of abdominal wall ¹	..	..	2	0·9
Scarring of feet and atrophy of nails ¹	..	..	5	2·3
Oedema of feet ¹	..	..	20	9·1
Pigmentation of nipple ²	..	..	23	10·5
" of body-wall ¹	..	..	8	3·6

¹ Extremities also cyanosed.² In majority extremities cyanosed.³ Cyanosed feet in 8 cases.⁴ Blue-black discoloration in 4.⁵ Cyanosed feet in 29 cases.⁶ Feet also cyanosed.⁷ Whole face 4, nose only 12, lips only 8.TABLE II.—*Relation of Cyanosis to Type of Mental Illness.***Observations at room temperature 62–65° F.*

Room temp. 62–65° F. (16·7–18·3° C.).		Number.	Proportion of mild to severe cyanosis.					
			Cyan. of extrem.		Mild cyanosis.		Severe cyanosis.	
			Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
M. Psychotics	Schizs.	166	10	6	9	90	1	10
	Affects.	70	2	2·9	2	100	..	..
	Defects.	64	4	5·6	3	75	1	25
	Total	300	16	5·3	14	87·5	2	12·5
F. Psychotics	Schizs.	90	57	63·3	42	73·7	15	26·3
	Affects.	66	13	20	10	76·9	3	23·1
	Defects.	64	25	39	16	64	9	36
	Total	220	95	43·2	68	71·6	27	28·4

* For distribution of cyanosis refer to Table I.

Comparison of male and female groups shows a preponderance of cyanosis in the latter, 43 per cent. of the female patients and only 5 per cent. of the male patients showing cyanosis, which was severe in 16 per cent. of the females and in less than 1 per cent. of the males.

No reason for the greater incidence of peripheral cyanosis among female patients was evident, the groups were examined under the same environmental conditions, their diet was the same and the physical appearance of the members of the female group compared favourably with that of the male patients. The only obvious difference between the two groups lay in the warmth of clothing worn by the male patients. Whereas men wore woollen socks, women had either cotton stockings or no stockings; the men had woollen suits, the women wore dresses of a lighter material. None of the women complained of cold and the weather was mild at the time, although indoor temperatures did not rise above 65° F.

To exclude the immediate effect of chilling on the appearance of their limbs, it was decided to examine a group of women patients at a higher indoor temperature.

Examination of 246 Female Psychotics at Room Temperature 82° F. (27·8° C.).
(See Tables III and IV.)

The patients were drawn from three wards, similar to those from which patients were taken for examination at ordinary room temperature, but those belonging to the refractory ward who were now included, were the most troublesome inmates of the female side of the hospital. The ages of patients included in this group varied between 25 and 65 years; 123 were between the ages of 25 and 50 years and 123 between 50 and 65 years.

Conditions of Observation and Clinical Findings.

These patients were observed in glass-roofed bathrooms of the hospital, during a spell of hot weather, before routine bathing. The moist heat of these rooms, which had a wall temperature of 82° F. (27·8° C.) was very oppressive. Groups of 40 to 60 patients were allowed to sit or wander about the communicating bathrooms for half an hour before they were undressed in small groups.

Unexpectedly, more striking cyanosis of the feet and hands was observed under these conditions than at lower room temperatures, and the proximal parts of the limbs were more often involved (see Table III). The limbs of

TABLE III.—*Cyanosis and Pigmentation in 246 Female Psychotics.*

Observations at room temperature 82° F.

Room temp. 82° F. (27·8° C.), steam-saturated air.		Number.	Per cent.
246 F. Psychotics	Cyanosed extremities	130	52·8
	Cyanosis of feet.—Mild	81	32·9
	" " Severe	49	19·9
	" of hands.—Mild ¹	52	21·1
	" " Severe ²	4	1·6
	" of face ³	31	12·6
	" below knees	106	43·1
	" of whole leg	8	3·3
	" of forearms	12	4·9
	" of breast ⁴	9	3·7
	" of abdominal wall	1	0·4
	Scarred toes, atrophic nails	2	0·8
	Oedema of feet	27	11
	Dark pigmentation of nipples	24	9·7
	Pigmented body-wall	28	11·4

¹ Feet also cyanosed in 47 cases.

² Cyanosis of feet in all cases.

³ Whole face 12, lips only 10, nose only 9.

⁴ In 6 cases limited to areola and adjoining skin.

all the patients were slightly flushed and it was evident that the depth of cyanotic discoloration was accentuated by engorgement of the skin; pigmentation, when present, was also more striking. It was not found possible to differentiate between "degrees" of cyanosis and "depth" of colour attributed to engorgement. Sir Thomas Lewis' standards of accuracy, based on a comparison with the basal skin colour, could not be attained, as the local change in appearance due to different illumination introduced an element of doubt whenever this evaluation was attempted. The term "severe cyanosis" was therefore retained, as previously defined, to denote any striking

discoloration of the skin of a dark purple or blue colour, without differentiating between basal colour and degree of cyanosis. Cyanosis of the extremities was present in 53 per cent. of the 246 female patients examined in a hot room and was severe in 20 per cent.

The Relation of Cyanosis to the Type of Mental Illness.

(See Tables II and IV.)

Patients were assigned to one of three clinical groups, according to the diagnosis made on admission, or at their last re-examination. All the classifications of mental illness are notoriously unsatisfactory and none are based on objective standards, but as the majority of these patients had been under observation for some months, or even years, the evolution of their mental disease helped to differentiate a schizophrenic from an affective psychosis. The three categories under which patients were classified, for the purpose of these observations, are the following: Schizophrenic illnesses, affective psychoses, mental defect (oligophrenics and dementes). The schizophrenic group included patients suffering from every form and every stage of mental illness in which thought disorder predominates. Catatonics and mischievous hebephrenics formed the bulk of the schizophrenic population in the so-called "refractory" wards; simple and arrested cases and paranoid patients came from wards for better behaved patients. The affective group comprised depressives and manic-depressives in depressive and hypomanic phases of the illness. The mental defective group included the patients in whom mental defect since infancy could be presumed and an equal number of patients in whom secondary dementia could not be excluded on available clinical evidence; it must, therefore, have included a number of deteriorated schizophrenics. In the case of female patients examined at higher room temperature, sub-grouping into ward-categories is shown (see Table IV). This subdivision into patients belonging to "refractory," "difficult" and "socialized" wards is a rough guide to their habitual behaviour, but not to the type of mental

TABLE IV.—*Relation of Cyanosis to Mental Illness and Behaviour.**

Observations at room temperature 82° F.

Room temp. 82° F. (27·8° C.). Steam-saturated air.		Num- ber.	Cyan. of extremis.		Proportion of mild to severe cyanosis.			
					Mild cyanosis.		Severe cyanosis.	
			Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
F. Schizs.	Socialized	32	12	37·5	9	75	3	25
	Refractory	54	45	83·3	24	53·3	21	46·7
	Difficult	22	14	63·6	5	35·7	9	64·3
	Total	108	71	65·7	38	53·5	33	46·5
F. Affects.	Socialized	17	4	23·5	2	50	2	50
	Refractory	23	7	30·5	5	71·4	2	28·6
	Difficult	17	6	35·3	6	100	..	..
	Total	57	17	30	13	76·5	4	23·5
F. Defects.	Socialized	29	11	38	9	81·8	2	18·2
	Refractory	12	5	41·6	4	80	1	20
	Difficult	40	26	65	15	57·7	11	42·3
	Total	81	42	51·8	28	66·7	14	33·3
Whole F. Psychotic group		246	130	52·8	79	60·8	51	39·2

* For distribution of cyanosis refer to Table III.

illness from which they suffer. In the case of both male and female patients who were examined at ordinary room temperatures, this subdivision is omitted, as the wards from which they were drawn were of a mixed type, and regrouping into ward-units was therefore useless.

When comparison is made of the occurrence of cyanosis in patients observed at ordinary and at higher room temperature it is evident that the incidence was highest in female schizophrenics and was almost equal in those examined at 82° F. and 62° F., 66 per cent. and 63 per cent. respectively in these two groups. Mental defectives occupied an intermediate position and affective patients showed the lowest incidence. The higher incidence of cyanosis in patients of the latter two groups when they were examined at higher room temperature, may be due to intensification of mild cyanosis by flushing of the skin. The highest incidence of peripheral cyanosis was found in so-called refractory schizophrenics. This observation concurs with the recognized frequency of cutaneous vascular changes in catatonics, as difficult, resistive and impulsive catatonics predominate among schizophrenics of the refractory wards. Many were resistive and tense at the time of their examination, assuming rigid attitudes and performing quick impulsive actions, such as pushing over chairs, or snatching and throwing small objects within their reach. In contrast, the schizophrenics who belonged to socialized wards conformed approximately with the conventional standards of good behaviour and gave a superficial impression of suffering from a milder illness. The few well-preserved paranoics showed no peripheral vascular disturbances, but restless and chronically hallucinated patients were usually affected. Schizophrenics from the wards for "difficult" cases occupied an intermediate position, both as regards their behaviour and the incidence of cyanosis.

On reviewing the case sheets of all these schizophrenics it was seen that a great many had passed through various phases of the illness and had been reclassified, in the course of years, under the various subdivisions of classical schizophrenia. Clinical labels appeared to reflect the evolution of the mental illness and the bent of past observers; this fact was sufficient to discourage any attempt to subdivide schizophrenic patients into groups corresponding to the usual clinical classification. It was interesting to note a relatively higher incidence of cyanosis in affective psychotics and defectives who belonged to "refractory," or "difficult" wards, compared with those who belonged to "socialized" wards. As some "hypomanics" and some "defectives" were possibly schizophrenics, it is impossible to estimate the true incidence of cyanosis in the refractory affective and defective patients.

Chronic and Transient Cyanosis of the Extremities.

(a) *Chronic peripheral cyanosis.*—The cyanosed appearance of the limbs of a number of patients was known to the staff of each ward. Those patients who were observed for months, and a smaller number observed for four years, showed little change in the appearance of their cyanosed limbs, and it was unknown for a case of severe cyanosis to clear between re-examination at two to four weeks' interval, except under the special circumstances noted

below. Some improvement, aided by tanning, was usual during the summer, while deterioration and chilblains were the rule in the winter; in very hot weather cyanosis was often more evident if the skin of the extremities was congested. Although spontaneous improvement was uncommon, the cutaneous condition remained reversible in every case, even when gangrene of the toes seemed imminent. A temporary measure of relief was always afforded (although improvement was seldom maintained) by any method which secured peripheral vasodilation. Improvement also followed after raising of the body-temperature by covering the patients with blankets and warming them with a cradle, particularly if their legs had been elevated. In a few cases dramatic relief of chronic cyanosis followed shortly after an electrical convulsion if a mental remission had been initiated by this treatment. During prolonged courses of insulin comas, and at the onset of spontaneous remissions, similar relief of cyanosis was observed in many cases. Examples of these clinical and experimental observations are given later under the appropriate headings.

(b) *Transient peripheral cyanosis related to chilling*.—Mild cyanosis resulting from moderate chilling is a common occurrence; the ease with which discoloration develops and the severity and persistence of the reaction vary within wide limits in normal persons. Psychotics show the same variability in their response to chilling, but schizophrenics and mental defectives are, as a class, prone to excessive vascular disturbances after exposure to moderate cold (see Table V). The female patients of this hospital may be regarded as permanently exposed to more rigorous environmental conditions than male patients owing to their lighter clothing; this circumstance may explain the liability of female patients to more severe and more enduring cutaneous reactions than those observed in male psychotics.

(c) *Evanescent form of peripheral cyanosis, unrelated to external temperature*.—A transient and recurring form of cyanosis of the hands, unrelated to changes of environmental temperature but clearly related to an increase in emotional tension, was frequently observed on the hands of young schizophrenic subjects of both sexes, in the early stages of their illness. This vascular change provoked by emotion was never observed in chronic schizophrenics and was rare in young patients who suffered from an affective psychosis or from mental defect.

The vascular responses to emotional stimuli of 18 young schizophrenics, 5 male and 13 female patients, were observed during the early months of their hospitalization. The average age of these patients was 24 years, the average duration of their overt illness was only $2\frac{1}{2}$ months. Fleeting cyanosis was noted on the hands of 17 of these 18 patients on many occasions during the first days of their stay in hospital, particularly when they were suffering from a confused or maniacal reaction. Cyanosis of the hands was occasionally seen to develop during the course of an interview, when these patients became tense, following a reference to their emotional problems. The reaction developed in a few minutes and faded within an hour, but a brick-red tint sometimes persisted for several days. The temperature of the hands bore no obvious relation to their cyanotic discoloration and varied between 24° C.

and 36° C. The skin of the feet was usually pale and not discoloured; its surface temperature was low, sometimes as low as 20° C. In a few cases in which cyanosis of the feet had developed it was less transient than that of the hands and bore no direct relation to emotional disturbance.

It seems likely that rapid vascular changes due to emotional causes result in cyanosis of the hands, whereas permanent vascular adjustments which accompany chilling, are in the course of months or years responsible for the cyanotic changes observed in the lower extremities.

The Relation of Cyanosis to Skin Temperature.

Cyanosed extremities usually felt cold to the hand, but this was not invariably the case. The relation of peripheral cyanosis to the temperature of the skin was investigated, at room temperature 62° F. (16.7° C.), in 90 male and 90 female psychotics, both groups containing 30 schizophrenics, 30 affective psychotics and 30 mental defectives (see Table V).

Surface temperatures were taken with 14-in., large bulb mercury thermometers, which were placed at the base of the first interdigital cleft of hands and feet. These thermometers gave comparable readings within 0.1° C. and were chosen after experimenting with thermocouples, as several patients distrusted wires and electrical apparatus. An attempt was made to achieve uniformity of conditions in recording skin temperatures, although air-conditioned rooms were not available and it was not considered justifiable to strip the patients under the circumstances. Patients wore their indoor clothing, and sat with bared forearms and legs, while their feet were placed on double blankets. They rested for at least half an hour before their skin temperatures were recorded. Moderate chilling resulting from immobility and exposure of the limbs caused the appearance of a mild cyanotic tint on extremities which had previously shown no cyanotic discoloration. This method of observation, adopted to minimize the difference in clothing of male and female patients, was the best that could be devised. It served incidentally to show the importance of warm clothes which sheathe the extremities; cyanosis of the feet was three to five times more frequent in male patients, after their limbs had been bared for half an hour at room temperature 62° F., whereas in female patients who wore lighter clothing (cotton stockings, or no stockings), the initial high incidence of cyanosis was not quite doubled by the same length of exposure. Under the conditions of observation the surface temperature and the appearance of the skin of the extremities of these patients indicate the response evoked by moderate chilling, rather than the habitual condition of their limbs when protected by clothing.

No simple relation was found between cyanosis and surface temperature and there was wide scatter of temperature-readings in all the groups examined. In two male patients for instance (a depressive and a schizophrenic), cyanosis of the feet was absent when the foot temperature was only 16° C.; in two others (a depressive and an imbecile), cyanosis of the feet was present when the foot temperature was 25° C. Similarly, a female imbecile showed no cyanosis when her foot temperature was 18° C., while several patients who

TABLE V.*—Cyanosis and Temperature of Extremities Before and After Exposure of Limbs to Room Temperature.

	LEFT FOOT.				RIGHT FOOT.				LEFT HAND.				RIGHT HAND.			
	Cyanosis.		Mean T.		Cyanosis.		Mean T.		Cyanosis.		Mean T.		Cyanosis.		Mean T.	
	Before exp. %.	After exp. %.	min.	exp. ° C.	Before exp. %.	After exp. %.	min.	exp. ° C.	Before exp. %.	After exp. %.	min.	exp. ° C.	Before exp. %.	After exp. %.	min.	exp. ° C.
Room temp. 62° F. (16·7° C.).																
30 M. schizs.	6·6	33·3	21·4	±0·7	10	30	21·8	±0·87	6·6	23·3	28·3	±0·55	10	23·3	28·6	±0·43
30 M. affecs.	..	20	23·6	±0·69	..	23·3	23·7	±0·69	..	10	28·7	±0·61	..	10	29·1	±0·59
30 M. defecs.	6·6	23·3	23·5	±0·72	6·6	20	22·7	±0·62	6·6	13·3	29	±0·64	6·6	13·3	28·9	±0·58
90 M. psychs.	4·4	25·5	22·9	±0·41	5·5	24·4	22·7	±0·42	4·4	15·6	28·7	±0·36	5·5	15·6	28·9	±0·32
30 F. schizs.	46·6	83·3	19·6	±0·43	46·6	83·3	19·6	±0·38	10	26·6	26·3	±0·56	10	26·6	26·6	±0·6
30 F. affecs.	20	30	24·1	±0·66	20	30	23·7	±0·62	3·3	10	29·0	±0·53	3·3	10	29·0	±0·56
30 F. defecs.	53·3	63·3	20·7	±0·54	50	60	21·1	±0·6	16·6	20	26·1	±0·66	16·6	20	26·4	±0·66
90 F. psychs.	40	58·8	21·5	±0·37	38·8	57·7	21·5	±0·38	10	18·8	27·1	±0·36	10	18·8	27·3	±0·37

Surface Temperature Related to Clinical Grouping.
Difference of means and probability level.

RIGHT FEET.						RIGHT HANDS.					
Mean T. °C.		Diff. of means.		Prob. level.		Mean T. °C.		Diff. of means.		Prob. level.	
Mean T. °C.	Diff. of means.	Prob. level.	Mean T. °C.	Diff. of means.		Prob. level.					
30 F. schizs.	19.6 ± 0.4					30 F. affecs.	23.7 ± 0.6	4.1 ± 0.7	< 0.01		
30 F. schizs.	19.6 ± 0.4					30 F. defecs.	21.1 ± 0.6	1.5 ± 0.7	0.02 - 0.05		
30 F. affecs.	23.7 ± 0.6					30 F. defecs.	21.1 ± 0.6	2.6 ± 0.8	< 0.01		
30 M. schizs.	21.8 ± 0.9					30 M. affecs.	23.7 ± 1.1	1.9 ± 1.1	0.1		
30 M. schizs.	21.8 ± 0.9					30 M. defecs.	22.7 ± 0.6	0.9 ± 1	0.4		
30 M. affecs.	23.7 ± 0.7					30 M. defecs.	22.7 ± 0.6	1.0 ± 0.9	0.3		

* The statistical evidence of observations summarized in the following tables was verified by M. E. J. Carr, B.Sc.

had foot temperatures of up to 29° C. suffered from cyanosed feet. These cases were, however, exceptional; the surface temperature of the feet was lower than 20° C. in all 4 male patients and in 18 of 29 female patients (63 per cent.) who had deeply-cyanosed feet. In patients with milder degrees of cyanosis, temperatures below 20° C. were found in only one third (6 of 18 cases) of the male patients, and in roughly one third (9 of 24 cases) of the female patients; in cases with no cyanosis, a foot temperature below 20° C. occurred in only 18 per cent. of the male patients (12 of 68 cases) and in 13 per cent. of the female patients (5 of 37 cases). Hand temperatures were higher than foot temperatures in every group; they showed as much scatter as foot temperatures and the absence of correlation of surface temperature and cyanosis was more evident in the case of hand temperatures.

Comparison of average surface temperatures of the hands and feet of 90 male with those of 90 female psychotics showed significantly lower values for the latter. The average foot temperature of the men was 22.8° C. $\pm$ 0.42 and of the women 21.5° C. $\pm$ 0.38; the average hand temperature of the men was 28.8° C. $\pm$ 0.34 and of the women 27.2° C. $\pm$ 0.36 (see Table VI).

Comparison of average surface temperature of cyanosed and non-cyanosed extremities of both male and female patients showed significantly lower temperatures for cyanosed limbs. The average temperature of the cyanosed hands of 13 male psychotics was 26.45° C. $\pm$ 0.74 and of the non-cyanosed

TABLE VI.—*Temperature of Cyanosed and Non-Cyanosed Extremities.*

		Males.		Females.		Difference between means °C.	Probability level.
		Number.	Mean temp. °C.	Number.	Mean temp. °C.		
Feet	Room temp 62° F (16.7° C.)						
	Cyanosed	22	20.3 $\pm$ 0.68	53	20.6 $\pm$ 0.42	0.3 $\pm$ 0.79	0.7
	Non-cyan.	68	23.6 $\pm$ 0.48	37	22.7 $\pm$ 0.62	0.9 $\pm$ 0.78	0.3
	Whole gp.	90	22.8 $\pm$ 0.42	90	21.5 $\pm$ 0.38	1.3 $\pm$ 0.57	0.02-0.05
			L. foot. 22.9 $\pm$ 0.41		L. foot. 21.5 $\pm$ 0.37		
			R. foot. 22.7 $\pm$ 0.42		R. foot. 21.5 $\pm$ 0.38		
Hands	Cyanosed	13	26.45 $\pm$ 0.74	18	22.7 $\pm$ 0.78	3.75 $\pm$ 1.11	<0.01
	Non-cyan.	77	29.0 $\pm$ 0.49	72	28.0 $\pm$ 0.38	1.0 $\pm$ 0.62	0.1
	Whole gp.	90	28.8 $\pm$ 0.34	90	27.2 $\pm$ 0.36	1.6 $\pm$ 0.50	<0.01
			L. hand. 28.7 $\pm$ 0.35		L. hand. 27.1 $\pm$ 0.36		
			R. hand. 28.9 $\pm$ 0.32		R. hand. 27.3 $\pm$ 0.37		

Difference Between Means and Probability Level.

		Non-cyanosed feet.		Cyanosed feet.		Difference betw. means. °C.	Probability level.
		Number.	Mean temp. °C.	Number.	Mean temp. °C.		
Males	.	68	23.6 ± 0.48	22	20.3 ± 0.68	3.3 ± 0.93	<0.01
Females	.	37	22.7 ± 0.62	53	20.6 ± 0.42	2.1 ± 0.72	<0.01

		Non-cyanosed hands.		Cyanosed hands.		Difference betw. means. °C.	Probability level.
		Number.	Mean temp. °C.	Number.	Mean temp. °C.		
Males	.	77	29.0 ± 0.49	13	26.45 ± 0.74	2.55 ± 1.22	0.02-0.05
Females	.	72	28.0 ± 0.38	18	22.7 ± 0.78	5.3 ± 0.85	<0.01

hands of 77 male psychotics $29^{\circ} \text{ C.} \pm 0.49$; that of the cyanosed hands of 18 female psychotics was $22.7^{\circ} \text{ C.} \pm 0.78$, and of the non-cyanosed hands of 72 female psychotics $28^{\circ} \text{ C.} \pm 0.38$. The average temperature of the cyanosed feet of 22 male psychotics was $20.3^{\circ} \text{ C.} \pm 0.68$ and of the non-cyanosed feet of 68 male psychotics it was $23.6^{\circ} \text{ C.} \pm 0.48$; the average temperature of the cyanosed feet of 53 female psychotics was $20.6^{\circ} \text{ C.} \pm 0.42$ and of the non-cyanosed feet of 37 female psychotics $22.7^{\circ} \text{ C.} \pm 0.62$. Comparison of the average temperature of non-cyanosed hands and feet of male and female patients, and of the average temperature of cyanosed feet of male and female patients showed no significant differences, but the cyanosed hands of 18 female psychotics showed a surface temperature significantly lower than that of the cyanosed hands of 13 male psychotics. This, together with the greater number of females with cyanosed limbs, accounts for the significantly lower average surface temperature of the hands and feet of female psychotics.

Within these larger groups, significantly lower readings were found for both foot and hand temperatures of 30 female schizophrenics and 30 female defectives compared with 30 female affective psychotics. Average temperatures of right and left limbs were recorded separately, to obtain parallel series of observations (see Table V). Very similar values were, however, obtained for the two sides. A difference of $0.5-1^{\circ} \text{ C.}$ in surface temperature of opposite hands, or feet, was frequently present (and in exceptional cases, differences up to 4° C. , for which no cause could be found) but averages for 30 or more patients showed little difference between right and left limbs (see Tables V and VI). Readings for right limbs are summarized here: The average surface temperatures of 30 female schizophrenics were, feet $19.6^{\circ} \text{ C.} \pm 0.38$, hands $26.6^{\circ} \text{ C.} \pm 0.6$; of 30 female affective psychotics, feet $23.7^{\circ} \text{ C.} \pm 0.62$, hands $29^{\circ} \text{ C.} \pm 0.56$, significantly lower values for female schizophrenics. No significant differences were found between the corresponding groups of male patients, although schizophrenics tended to have lower foot temperatures than affective psychotics.

A frequent, but not invariable association of low surface temperature and peripheral cyanosis was demonstrated by these observations.

The Effect of Environmental Temperature on Cyanosis and Foot Temperature of Affective and Schizophrenic Patients.

Twelve unselected female affective psychotics and 12 unselected female schizophrenics were observed at room temperature 75° F. (23.9° C.), and again at room temperature 60° F. (15.6° C.) (see Table VII). At room temperature 75° F. , almost identical average foot temperatures of 32° C. were found for the patients belonging to these two groups (a fortuitous circumstance); when the same patients were re-examined at room temperature 60° F. , there was a marked difference between the average foot temperature of the two groups, that of the schizophrenic group dropping more than 6° C. below that of the affective group. In both affective psychotics and schizophrenics cyanosis was more common at a higher room temperature, when

TABLE VII.—*The Foot Temperature of Affective Psychotics and Schizophrenics at Room Temperature 75° F. and 60° F. (23·9° and 11·6° C.).*

Room temp.	Mental illness.	Number of patients.	Mean temp. feet ° C.	Cyand. feet. Number of cases.
75° F. (23·9° C.)	Affective psychotics	12	32·05 ± 0·93	5
	Schizophrenics	12	32·06 ± 0·77	11
60° F. (15·6° C.)	Affective psychotics	12	23·37 ± 1·06	2
	Schizophrenics	12	16·95 ± 0·34	9

Difference of means of foot temp. at high and low room temp.:

Affective psychotics $8·68 \pm 1·3$. Probability level $< 0·01$.

Schizophrenics $15·1 \pm 0·84$. Probability level $< 0·01$.

Difference of means of fall of foot temp. in affective psychotics and schizophrenics:

$6·42 \pm 1·59$. Probability level $< 0·01$.

the skin was congested, but the incidence of cyanosis was greater in the case of schizophrenics, not only with higher but also with lower environmental temperatures. Similar observations were made on frequent occasions; schizophrenics who had a low foot temperature compared with that of affective patients, when they were both examined in chilly surroundings, had the same foot temperature as affective patients when both were observed in warmer surroundings. Hand temperatures showed greater variability and it was not found possible to obtain comparable readings; immobility of the hands could not be secured, the fists were frequently closed, or the hands were warmed against the thighs. Both low and average hand temperatures were encountered in schizophrenic patients, apparently unrelated to atmospheric conditions.

Skin Temperature Gradients.

The skin temperature gradients of 12 female schizophrenics who had a low foot temperature were compared with the temperature gradients of 30 normal individuals of both sexes, published by R. L. Richards (5) (see Table VIII). The average knee temperature of these patients was higher and their toe temperature lower than that of the normal controls. The lowest toe temperature of the normal group was 16° C., that of the schizophrenics 13° C. Even in patients who had an extremely low foot temperature, knee temperatures were never below the minimal "normal" value of 25·6° C., given by Richards; in several cases they were well above the normal average value of 28° C.

Routine foot temperatures were taken, as has already been stated, by placing the bulb of the mercury thermometer at the base of the first interdigital cleft; this was easier than balancing it against the tip of the big toe and avoided the necessity of handling the patient's foot, thereby altering its surface temperature.

The temperature of the tip of the toes was recorded in those patients in whom very low foot temperatures were encountered; it was usually between $1\frac{1}{2}$ and 4° C. lower than that of the root of the toes. The temperature of the dorsum of the foot was either the same as that of the root of the big toe or a degree or two higher, and the ankle temperature was 1–3° C. higher than that of the dorsum. The steep gradient of the surface temperature between

TABLE VIII.—*Surface Temperature Gradients of Schizophrenics and Normal Subjects.**

Room temp.	Number of cases.	Mean temperatures ° C.						Toe-knee difference
		Tip of Hallux.	1st space.	Dorsum of foot.	Ankle.	Knee.		
64° F. (17·8° C.)	12 F. schizs.	18·7 ±0·05	20·1 ±0·75	21·2 ±0·71	22·3 ±0·68	30·8 ±0·25		12·1 ±0·50
64-71° F. (18-22° C.)	30 Norm. controls	20·3	..	24·3	26·4	28·1		7·8

* Mean temperature readings for normal subjects given by Richards (5).

the knee and ankle was a constant feature in patients with a low foot temperature.

The Relation of the Patient's Age to the Incidence of Cyanosis.

In order to ascertain whether cyanosed extremities occurred more frequently in older than in younger patients, as might well be the case if they were associated, for instance, with cardio-vascular degenerative lesions, or with chronic mental illness, the total psychotic population of 300 male and 400 female patients was subdivided into two age groups, comprising those under and those over 50 years of age. The incidence of peripheral cyanosis in 235 women aged less than 50 was found to be 57 per cent., and in 165 women aged more than 50 it was only 38 per cent. The incidence in 196 men under 50 was 6 per cent., and in 104 men over 50 it was 4 per cent.

The lower incidence of cyanosis in patients over 50 years of age can be attributed (in part at least) to a greater number of affective psychotics and socialized schizophrenics in the higher age group, these patients being less prone to cutaneous vascular disturbances than other schizophrenics or mental defectives.

The Relation of Habitual Activity to Chronic Cyanosis of the Feet.

The relation of chronic cyanosis to habitual activity was investigated in 90 male patients and in 100 female patients. The male group was the same as that previously mentioned, while the female group was enlarged by the inclusion of ten other cases. The degree of bodily activity of all these patients was observed and was also discussed with the staff of the wards to which these patients belonged. These observations are summarized in Table IX. The active patients are subdivided into two groups, very active (V.A.) and active (A.). The very active group includes the good workers, patients who are employed continuously on manual work, either inside the hospital or in its grounds, gardening, floor polishing, scrubbing, laundry-work, coal deliveries etc. It also includes some overactive patients whose activities are not useful and who spend their time restlessly pacing the wards or the courts of the hospital. The second group consists of less active patients who only do a little manual work, or do it grudgingly and sporadically, they lay tables, sweep floors, deliver tea, polish door handles, etc. Inactive patients are subdivided into those who are habitually standing (St.) and those who are habitually sitting (Si.). Many of the former had stood almost immobile,

TABLE IX.—*Cyanosis of the Extremities, Related to the Mental Illness and the Habitual Mode of Activity, of 90 Male and 100 Female Psychotics.*

Room temp. 62° F. (16·7° C.).		Habitual activity of patients.											
		Very active.			Active.			Standing.			Sitting.		
Cyanosis of FEET.		Sch.	Aff.	Def.	Sch.	Aff.	Def.	Sch.	Aff.	Def.	Sch.	Aff.	Def.
Severe	1 M.	..	..	..	..	..	..	1	..	..	..	..	..
	20 F.	..	..	1	3	1	2	1	..	1	6	2	3
Mild	3 M.	..	..	..	..	..	..	..	..	2	1	..	..
	25 F.	2	..	1	6	1	4	1	..	..	2	3	5
None	86 M.	14	24	17	1	4	4	7	1	2	6	1	5
	55 F.	..	11	9	7	10	3	..	..	..	4	5	6
Cyanosis of HANDS.													
Severe	1 M.	..	..	..	..	..	..	1	..	..	..	..	..
	2 F.	..	..	..	..	..	..	..	..	..	1	..	..
Mild	3 M.	..	..	1	..	..	..	1	..	1	..	..	..
	5 F.	..	..	..	..	..	3	..	..	1	..	..	1
None	86 M.	14	24	16	1	4	4	6	1	3	7	1	5
	93 F.	2	11	11	16	12	6	2	..	..	11	10	12

Very active.—Habitually working.

Active.—Light work, walking about.

Standing.—Habitually standing immobile.

Sitting.—Sitting or reclining immobile.

Sch.—Schizophrenic.

Aff.—Affective illness.

Def.—Mental defective.

seldom shifting their positions during the whole day for weeks or months preceding this survey. They stood either unsupported or propped-up against a wall or a piece of furniture. Their postures were maintained, apparently, without fatigue, for many hours and some of them could only be shifted by being pushed or pulled. Several of them had to be fed standing as they refused to sit down for a meal. When forced to lie down on their bed at night, they frequently assumed rigid postures and held their head raised above their pillow, until they finally relaxed on falling asleep.

Inactive sitting patients spent the greater part of the day sitting on the edge of a chair, or took a few aimless steps before settling again on a chair or bench. Others preferred to crouch on the floor whenever they were allowed to do so.

There were 79 very active patients, 55 males and 24 females; 46 active patients, 9 males and 37 females; 16 patients who were habitually standing, 13 males and 3 females; and 49 patients who were habitually sitting, 13 males and 36 females.

Severe cyanosis of the feet was present in 1 very active and in 6 active female patients and was absent in all very active and active male patients. It was present in 1 male and 2 female patients who were habitually standing and in 11 female patients who were habitually sitting.

Milder degrees of cyanosis of the feet occurred in 3 very active and 11 active female patients, in 1 female and 2 male patients who were habitually standing and in 10 female and 1 male patient who were habitually sitting. The patients who showed no cyanosis of the feet included the majority of the very active workers, 55 men and 20 women, also 9 men and 20 women who were employed on light or occasional work. An unexpected finding was the absence of cyanosis of the feet in 10 male patients who were known to have stood almost immobile throughout the day for weeks, previous to the time of their examination, and in 12 male and 15 female patients who were habitually sitting and rarely shifted their position.

The Effect of Work on Cyanosis.

Twelve female psychotics, 8 schizophrenics, 2 manic depressives and 2 mental defectives, who were all suffering from cyanosis of the feet, were vigorously exercised for 10 minutes, each patient jumping ten or more times on and off the seat of a chair, before running round some tables. This "game" was enjoyed by most of the participants, but was found exhausting by some patients, as a hot day, with a room temperature of 75° F. (23·9° C.), had been chosen for this test. Foot temperatures were taken before and after exercise (see Table X).

TABLE X.—*The Effect of Work on Cyanosis and Foot Temperature of 12 Female Psychotics.*

Room temp	Before exercise.		After exercise.		Difference of means.	Probability level.
	Cyanosed feet.	Mean foot temp.	Cyanosed feet.	Mean foot temp.		
	Number of patients.	° C.	Number of patients.	° C.		
75° F. (23·9° C.)	12	25·21±·16	6	26·25±0·9	1·0±1·78	0·5-0·6

The average foot temperature of the whole group was 1° C. higher after exercising, gains of 0·5°-6° C. being recorded in 9 patients, no change in two and a drop of 1·5° C. in another.

Cyanosis was completely relieved by exercise in 6 patients (4 of whom showed a rise of foot temperature and 2 no change); it was partly relieved in 5 (4 of whom showed a rise of temperature and 1 a fall) and it remained unchanged in 1 chronic schizophrenic, whose foot temperature was 2° C. higher after exercise. In 2 patients who showed relief of cyanosis no rise of foot temperature occurred, while in one patient, who was partly relieved, a drop of foot temperature of 1·5° C. was registered after exercise.

The Effect of Gravity on Cyanosis and Foot Temperature.

In patients with severe cyanosis the skin of the feet often presented a turgid engorged appearance and there was some swelling of unsupported parts of the foot, particularly of the dorsum, in patients who wore house shoes. When the shoes were removed the darker cyanotic colour of the dorsum spread forwards and downwards until the whole foot was uniformly dark. In other patients the support given by cotton stockings was sufficient to assure an almost normal appearance of the skin, so that when the stocking was lowered the colour of the leg and foot became darker and the pattern of cutaneous venules became visible. On the other hand, relief or partial relief of cyanosis was afforded by elevating the legs. This was the posture adopted to alleviate severe cyanosis in female patients whenever gangrene of the toes appeared imminent.

The following observations were made to estimate the importance of postural factors in the relief of cyanosis of the feet.

Experimental Procedure.

Twenty female psychotics who suffered from cyanosis of the feet were examined after they had rested while sitting for half an hour at room temperature 64° F. (17.8 C.) (see Table XI). They were divided into two groups, those with low foot temperatures averaging 17° C. (the lowest temperature was 15° C. and the highest 19° C.), and those with higher foot temperatures averaging 23.6° C. (the lowest temperature was 20° C. and the highest 35° C.). After surface temperatures had been recorded, the legs of these patients, who were sitting on chairs, were raised (first one and then both) on the seat of a chair placed in front of them.

The immediate result of raising one leg was lightening of cyanosis of that foot and a small initial fall of temperature, which was more frequently observed in patients who had warmer feet. In the group of 10 patients with warmer feet there was an average initial fall of temperature of 0.5° C. $\pm$ 0.16, 7 patients registering a fall, 2 no change and 1 a rise of 0.5° C.

The 10 patients with colder feet showed only a very small average fall of 0.25° C. $\pm$ 0.11, the temperature falling in 4 and remaining unaltered in 6 cases.

At the end of 10 minutes' elevation of one leg, there was a slight gain in average temperature (as compared with initial temperature) in patients of both groups. A gain of 0.75° C. $\pm$ 0.29 was registered in those with warmer limbs, 8 patients registering gains and 2 regaining their initial foot temperature. An average gain of 0.9° C. $\pm$ 0.09 occurred in patients with colder limbs, their surface temperature rising from 0.5 to 2° C. The temperature of the dependent foot was unexpectedly found to show a slight rise also in half the cases, the gain, when it occurred, being higher for 6 patients with colder feet (average gain 0.65° C. $\pm$ 0.17) than for 5 patients with warmer feet (average gain 0.35° C. $\pm$ 0.15). After the second foot had been raised a further slight rise of temperature occurred in 6 patients with colder and in 2 with warmer feet, the other patients registering now a slight fall of temperature.

There was some relief of cyanosis in all but 4 patients (2 in each group), and in 2 patients with warmer feet the colour of the feet became normal after elevation.

After lowering the feet cyanosis again developed and was marked in all cases, but was preceded in a few patients by a preliminary reddening of the skin and a further slight rise of temperature of 0.5-1° C., this rise being obviously due to a partial reactive hyperaemia. After 15 minutes the original depth of cyanosis had recurred in all; the temperature of 7 patients who had initially had colder limbs remained elevated for some time and only reached its low initial level one hour later.

The transient fall of cutaneous temperature after elevation of the leg coincided with decreased cyanosis and was interpreted as the result of decongestion, following improved venous drainage. Coincident arteriolar constriction could not be excluded, but it could hardly have accounted for improved colour of the skin. The secondary rise of temperature, after elevation of the limbs, is due presumably to a diminution of those physiological vaso-

TABLE XI.—Effect of Raising the Legs on Surface Temperature and Cyanosis of Feet of 10 Female Psychotics with Low, and 10 with Higher Initial Foot Temperatures.

No. of cases.	Room temp. 64° F. (17·8° C.).	Mean temp. feet at onset.		Number of cases with cyanosis of feet.	Right leg raised.						Left leg also raised.						Relief of cyanosis.		Mean temperature, hands.		
		L. foot. °C.	R. foot. °C.		90 sec. reading.		10 min. reading.		Left foot.		Right foot.		Left foot.		Right foot.		Complete	Partial.	At onset. °C.	After legs raised. °C.	Loss or gain. °C.
10	15-19	17	17	10	Mean T. °C.	Mean loss. °C.	Mean T. °C.	Mean gain. °C.	Mean T. °C.	Mean gain. °C.	Mean T. °C.	Mean gain. °C.	Mean T. °C.	Mean gain. °C.	Mean T. °C.	Mean gain. °C.	0	8	24·65	24·45	0·2
		±0·43	±0·41		±0·43	±0·11	±0·36	±0·17	±0·34	±0·09	±0·33	±0·35	±0·41	±0·28	±0·41	±0·28			±1·11	±1·18	±0·45
10	20-35	23·60	23·9	10	23·4	0·50	23·95	0·35	24·65	0·75	23·85	0·25	24·60	0·70	24·60	0·70	2	6	28·37	28·45	0·08
		±1·55	±1·57		±1·47	±0·16	±1·45	±0·15	±1·59	±0·29	±1·44	±0·2	±1·59	±0·22	±1·59	±0·22			±0·85	±0·85	±0·27

* Individual measurements compared with initial foot temperatures.

constrictor impulses which come into play when the erect posture is assumed, or when the legs are dependent.

Small differences in the average foot temperature of these two groups of patients are not significant.

The Part Played by Antigravity and Temperature Regulating Mechanisms in the Incidence of Cyanosis.

The following observations were made in an attempt to differentiate between the part played by antigravity and temperature regulating mechanisms in the development of peripheral cyanosis.

Experimental Procedure.

Fifteen female patients who suffered from severe cyanosis of the feet were observed after resting at lower and at higher room temperature and the effect of elevation of the feet, on the depth of cyanosis and foot temperature, was noted under both environmental conditions; 9 of these patients were chronic schizophrenics and 6 were affective psychotics (see Table XII). At room

TABLE XII.—*Effect of Raising the Legs on Surface Temperature of Cyanosed Feet.*

Room temp.	Number of pts.	Cyanosed FEET. Number of cases.	Mean temp. before raising FEET. ° C.	Mean temp. after raising FEET. ° C.	Mean loss. ° C.	Relief of cyanosis	
						Compl.	Partl.
50° F. (10·0° C.)	15	15	15·25 ± 0·4	14·7 ± 0·50	0·55 ± 0·17	0	6
64° F. (17·8° C.)	15	15	24·9 ± 1·12	23·85 ± 1·12	1·05 ± 0·25	4	11

temperature 50° F. (10° C.) the foot temperature of every patient was lower than 19° C. (average temperature 15·25° C. ± 0·4) and at room temperature 64° F. (17·8° C.) it was higher than 19° C. (average temperature 24·9° C. ± 1·12). All these temperature readings were fairly evenly spaced between extreme values of 14° C. and 34° C.

After the legs of these patients had been raised, by resting their feet on the back of a low chair (an angle of about 15° above horizontal level), the foot temperature fell in all but 3 patients, who showed no change. The fall was slightly greater in the majority of patients with warmer limbs (average fall of 1·05° C. ± 0·25) than in those with colder limbs (average fall of 0·55° C. ± 0·17).

A much more striking difference between the two groups was a marked relief of cyanosis in patients with higher foot temperatures, compared with those with colder limbs, who showed little change in the appearance of their feet after these had been raised. Before elevation cyanosis was severe and approximately equal in all patients, under both conditions of observation. After elevation, 4 of the group observed at higher room temperature were completely relieved, the others were very much improved, while none of the patients in the colder room were completely relieved and only 6 showed slight improvement.

Disappearance of cyanosis after raising the feet (which occurred in patients with warmer limbs), shows the importance of postural factors in the development of cyanosis; the failure of patients with colder limbs to show similar improvement indicates the importance of the second mechanism which underlies cutaneous vascular changes, a diminution of cutaneous blood flow, for the purpose of conserving heat; the adequacy of the peripheral blood supply may be endangered by the thermal requirements of the organism as a whole.

Relief of Severe Cyanosis and of Threatened Gangrene of the Toes by Raising the Feet and Warming the Body.

Two female hebephrenic patients, one aged 45, the other 37, were reported on separate occasions to show black discoloration of their toes. On inspection their feet were found to be deeply cyanosed and moderately swollen; the tips of the first and third toes of the right foot of one patient and of all the toes of the second patient were black, the remaining parts of the feet were a deep purple colour and mottled. No pulsation could be felt in the dorsalis pedis or the posterior tibial arteries and there was no bleeding after a toe had been pricked. Pulsation in the popliteal arteries was normal. Both patients were put to bed; their legs, wrapped in wool, were elevated to 30 degrees and rested on pillows. The toes were left exposed, while the patients were warmed by an electric cradle placed over the abdomen. After two days pulsation could again be felt in the arteries of the feet and cyanosis was much less marked. A few scabs on the terminal phalanges of the toes of the second patient separated a few days later with little loss of tissue; within a week the colour of the feet of both patients was normal while they were lying down and only mildly cyanotic when they were standing up. The first of these two patients succumbed a year later to a respiratory infection. During the last days of her illness the circulation of her feet was again very deficient and gangrene of the toes seemed imminent, but she died before this had developed. On microscopical examination the arteries of her feet and legs were normal, the digital vessels and dorsalis pedis arteries showed no abnormalities, with the possible exception of slight thickening of the muscular coat of these vessels.

Relief of Cyanosis by Experimental Vasodilatation.

(a) *Reflex vasodilatation by warming an indifferent limb.*—(See Table XIII) (Chart I). Reflex vasodilatation was induced by this method in 7 female

TABLE XIII.—*Reflex Vasodilatation by Warming Indifferent Limb in Water-Bath 45° C.*

Room temperature 68° F. (20° C.).

Mental Illness.	Number of cases.	Cyanosis of FEET. No.	Mean temp. 1st toes. ° C.	Onset of vasodil. mins.	Full vasodil. mins.	Mean temp. aft. vasodil. ° C.	Temp. gain. ° C.
Affec.	2		21.25	16	33.5	30.5	9.25
Schiz.	3	3	± 0.18	± 4.3	± 2.5	± 1.43	± 1.6
			21.59	42.6	67	31	9.41
			± 0.9	± 3	± 3.3	± 1.20	± 1.9
Schiz. remissn.	2		26.5	7.5	25	34.75	8.2
			± 1.07	± 1.8	± 7.1	± 0.18	± 0.89

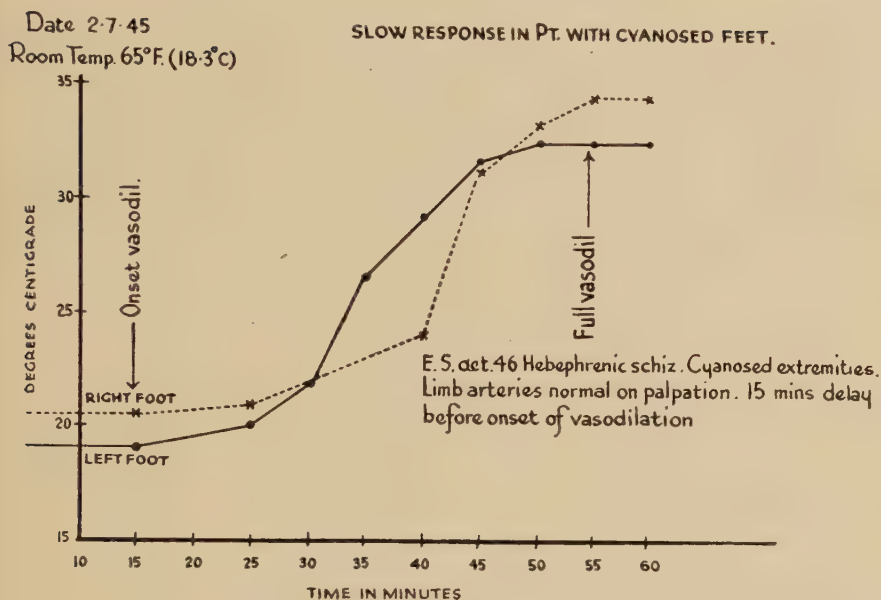


CHART I.—Reflex Vasodilation. Foot temp. (1st cleft) before immersing and after immersing left forearm in water-bath 45° C.

patients, 3 schizophrenics (2 hebephrenics and 1 catatonic) who had deeply cyanosed feet, 2 affective psychotics and 2 patients with schizophrenic remissions who showed no cyanosis of the extremities.

After resting on a couch at room temperature 68° F. (20° C.) the left arm of each patient was immersed in a water bath maintained at 45° C. Foot temperatures were taken every 3 minutes until a maximum rise had been recorded; reflex vasodilatation was shown by lifting of cyanosis and reddening of the skin. Relief of cyanosis was complete in every patient in whom it had been present. Rises of foot temperature of 7° C. and 11.5° C. occurred in the two affective psychotics and rises of 7 to 14° C. in the 5 schizophrenics. The highest rise (14° C.) occurred in the schizophrenic who had shown the lowest initial foot temperature and deepest cyanosis. The time of onset of vasodilatation, as gauged by a rise of foot temperature, was very much delayed in schizophrenics with cyanosed feet and heating of the second arm was necessary in one of these patients, as no rise of foot temperature had occurred after 45 minutes' immersion of one arm. In the 2 affective psychotics and the 2 patients with a schizophrenic remission vasodilatation was more rapid. Cyanosis, when present, cleared very gradually and at first only in patches; beginning in the leg the flush extended slowly to the feet and toes, finally to the heel and the dorsum of the foot. Areas of cyanotic skin left behind the advancing erythema cleared gradually. In the 2 affective psychotics and in the 2 patients with schizophrenic remissions vasodilatation occurred almost simultaneously over the whole leg and foot and then increased in intensity to a full reaction. In a case which is not included above, a female hebephrenic with deeply cyanosed limbs, reflex vasodilatation was hastened by inhaling amyl nitrite before immersion of her arm in the water bath. Although vaso-

dilatation was not evident before immersion, it developed 10 minutes later, much earlier than the average time for cyanosed extremities; a maximum rise of foot temperature of 15° C. was recorded in this patient.

(b) *Reactive hyperaemia*.—Reactive hyperaemia after temporary occlusion of the femoral artery, by a tourniquet applied to the thigh for 10 minutes, gave complete relief of cyanosis by vasodilatation in 5 schizophrenic female patients who had severe cyanosis of the feet. Full vasodilatory reactions were also observed in 5 other schizophrenics (3 males and 2 females) and 4 affective psychotics whose feet were not cyanosed (see Table XIV).

TABLE XIV.—*Reactive Hyperaemia after Release of Tourniquet Applied to Thigh.**

Room temp. 68° F. (20° C.).	Cyanosis of FEET. Number of cases.	Mean foot temp. at onset. ° C.	Hyperaemia.		Mean foot temp. after vasodil. ° C.	Relief of cyanosis. No.
			Onset sec.	Full sec.		
Schizophr. (5 fem.) .	5	23	25.6	105	..	5
		±1.02	±11.9	±29.3		
Schizophr. (3 M. and 2 F.)	0	24.5	10.1	30.4	..	..
		±0.95	±1.36	±4.4		
Whole schizophr. group	5	23.75	17.85	69.5	28.1	5
		±0.73	±5.6	±19.3	±0.53	
Affective psychotics .	0	25.87	4.5	22.5	33.5	..
		±2.38	±0.43	±0.79	±0.56	

* The leg was warmed for 10 minutes in water-bath 35° C. and then elevated before the tourniquet was applied.

The tourniquet was applied after the leg had been warmed for 10 minutes in a water bath at 35° C. The leg was then dried, elevated and massaged to empty the veins. The pressure in the cuff was rapidly raised above systolic pressure, before the limb was again lowered, warmed and dried. The pressure was then released. In 5 schizophrenic patients, whose feet were cyanosed at the onset, the reaction developed slowly and was patchy and incomplete at first, although the feet of these patients had the same blanched appearance after being warmed, elevated and massaged, as those of patients with no initial cyanosis; cyanosis recurred as soon as vasodilatation subsided. In schizophrenic patients, whose limbs were not cyanosed at the onset, hyperaemia was earlier but it was more gradual than that which occurred in affective psychotics. In patients who showed delayed reactions the erythematous areas were at first scattered; they coalesced later and gradually spread downward, from the leg to the foot.

Relief of Cyanosis During Mental Remission.

Remission Initiated by Electroconvulsive Treatment (E.C.T.).

Fading of peripheral cyanosis in a catatonic patient after the fourth E.C.T., which initiated a mental remission, drew attention to the possible relation of these two events. Twelve other patients who had cyanosed limbs and who were considered suitable for E.C.T. were then observed, 6 female schizophrenics (5 catatonics and 1 hebephrenic) and 6 female depressives. These patients had deeply cyanosed feet and less marked discoloration of their hands and

legs before treatment was commenced. Mental remissions occurred after 2-6 treatments in 5 of the 6 depressives; temporary remissions occurred in all 5 catatonics. Cyanosis disappeared with the onset of mental improvement but recurred when the mental condition again deteriorated, 5 days to 3 weeks later in the case of the catatonics, 4 weeks later in that of the only depressive patient who relapsed under observation. One depressive and the only hebephrenic of this group showed no mental change and no improvement of peripheral cyanosis after 12 E.C.T.

Mental changes in these depressive patients on the first day of their remission were definite and characteristic, although they were less striking than those observed in stuporous catatonics. Mental improvement became evident about 2-8 hours after successful treatment, as soon as the patients had recovered from mild confusion, torpor or agitation which followed E.C.T. In depressive patients the facial expression became brighter and the posture more normal. The patients showed renewed interest in their neighbours, answered questions and smiled naturally, in striking contrast with their previous lack of interest, silence and gloom. Examination of the limbs at this time and while the remission lasted showed absence of cyanosis. The skin of the legs and feet looked normal, or showed only a patchy dark red discoloration when the patients were standing.

In recovered catatonics the mental changes were similar in all cases, but were most striking in the worst case, a description of which follows. This patient was a teacher aged 33 who had a bad family history; her mother and brother were both in mental hospitals. She first broke down when she was 25. She had been in hospital for 4 years and had been stuporous for 3 years, ever since a course of insulin comas had had to be interrupted owing to deepening stupor. Amphetamine and sodium amytal medication had both been tried, without success. She had remained stuporous, mute and resistive and during the preceding 6 months she had been lying curled-up in bed with clenched fists, immobile, except for sucking movements of her lips. She was terribly emaciated, although she had been spoon-fed regularly. Her muscles were wasted and taut, her legs and hands deeply cyanosed. A fatal termination seemed imminent, but as the action of the heart and kidneys remained satisfactory the urgent request of her relatives for treatment by electroconvulsion had been granted, after the risks and the probable hopelessness of this treatment had been explained to them.

A first convulsion was well tolerated and brought no change in the patient's condition. On the following day, about 3 hours after the second convulsion, her expression underwent a striking change, became normal, amiable and animated. She looked round the ward in astonishment and asked, "Where am I?" She was now able to answer simple questions ("How are you?" etc.), and seemed entertained and puzzled by this new experience. She said that she must have been sleepy as she could only remember her admission (4 years previously). When reminded of events occurring after that date she recognized some of them, recalling visits of her husband and a change of ward. In spite of great weakness she was able to eat for the first time with evident pleasure and ravenous appetite. A few hours later she wrote a letter

to her husband, in a shaky hand, saying that she was now well and asking to be sent news of everyone at home. The cyanosed colour of her limbs had faded with the onset of this mental improvement. The limbs looked normal although the patient had not moved from her bed.

This patient's bright facial expression and mental clarity lasted only 5 days; they were succeeded by slowing-up of all mental processes and a gradual sinking-back into a semi-stuporous condition, from which she could at first be roused. Although there had been little increase of bodily activity during her brief remission, the movements of her face and arms had been more normal and she had unclenched her fists as far as her shortened tendons would allow. After the fifth day her face set again in rigid lines which now suggested terror; her right arm was held flexed and elevated above her head, with clenched fist; her feet, legs and hands were again deeply cyanosed.

The other catatonic patients had similar brief intervals of almost normal mental life during their short remissions following E.C.T. None of these patients showed much initiative, depth of affect, or sustained power of reasoning during their remissions, and all relapsed into stupor after 5 to 21 days. Their limbs, which had assumed a normal appearance during the remission, showed renewed cyanotic discoloration when the mental condition deteriorated.

The exact moment at which cyanosis cleared was not witnessed; its presence after an unsuccessful E.C.T., and its disappearance with the onset of a remission were ascertained on many occasions: the cyanotic colour lightened as the immediate result of the convulsion and failed to return in those patients who had a remission.

The whole process was witnessed again in second and third remissions following E.C.T., particularly in the case of 3 catatonics who had frequent relapses. One girl who responded to E.C.T. whenever she sank into stupor, had 6 successive remissions at a few weeks' interval; they became shorter and shorter until treatment was finally abandoned. Her cutaneous circulation remained a faithful indication of her mental state; her legs were a striking heliotrope shade when she was stuporous, resistive and mute, but had a normal appearance when, after a further convulsion her facial expression became pleasing and her speech rational, but puerile. She then assumed a reclining position on a couch and chatted amiably with her ward-mates (Chart II).

The common element in the mental remission of schizophrenic and depressive patients was lessening of mental tension, "Entspannung." Vascular changes coincided with this mental change and with decreased muscle tension, when this had been present, but they did not always synchronize with increased bodily activity. In some cases in which muscular rigidity had not been prominent before treatment there was no obvious change in muscle tone after a remission.

Relief of Cyanosis with the Onset of Spontaneous Remission.

Seven female schizophrenics who suffered from peripheral cyanosis (6 hebephrenics and 1 catatonic), whose illnesses had lasted from 3 months to 15 years, had spontaneous remissions under observation. Their mental

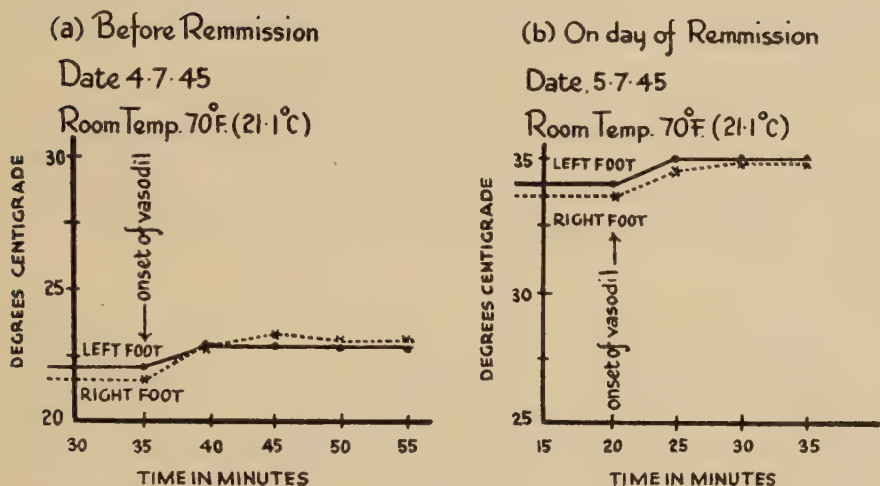


CHART 2.—Reflex Vasodilation. (a) before Remission and (b) on day of Remission.

improvement coincided with clearing of peripheral cyanosis, which had been severe in 4 patients and milder in others. In 3 of these patients (including a woman who had been in hospital 15 years) mental improvement was sudden and synchronized with improvement of the peripheral circulation, while in the other cases mental recovery was more gradual and it was therefore impossible to state exactly when the cutaneous circulation had improved; the mental change and the absence of cyanosis were noted at the following fortnightly routine examination. As these 7 patients had all been very restless during the months which preceded their remissions it is unlikely that the disappearance of cyanosis can be attributed, in their case, to increased physical activity; their remissions were characterized by lessened bodily activity and diminution of tension.

Relief of Cyanosis by Insulin Treatment, Nicotinic Acid and Nerve Blocking.

1. *Insulin shock therapy.*—No consecutive observations were made on the relief of peripheral cyanosis during prolonged courses of insulin treatment, but at least 14 patients were known and others were reported to have been relieved at some time during a course of insulin comas. No evidence of the persistence of cyanosis after a good remission could be found on looking up discharge notes of patients who had recovered after insulin treatment, or on discussing the question with the medical and nursing staffs of insulin treatment wards. As the gradual improvement in mental and physical condition during insulin treatment is accompanied by increased bodily activity it would be difficult to attribute decreased cyanosis to the direct effect of a remission.

2. *Nicotinic acid administration by oral route.*—Eight schizophrenics and 8 depressive female patients who suffered from peripheral cyanosis were given 200 mg. nicotinic acid by mouth daily for 7 days. In every case some relief was afforded by the ensuing vasodilatation; in a few cases relief persisted

for some days after cessation of this treatment, but there was no permanent benefit to any patient. Oral nicotinic acid was found useful when it was given to avert chilblains in patients subject to this condition.

3. *Procaine blocking*.—Blocking of peripheral nerves by the injection of 2 per cent. procaine hydrochloride caused vasodilatation of the peripheral vessels which receive their vasoconstrictor supply from “blocked” nerves. Local anaesthesia and transient relief of cyanosis of the fingers or toes, lasting from 5–30 minutes, was observed in 6 patients in whom nerve blocking was carried out.

Observations on the State of the Arteries of the Limbs and of the Retinal Arteries of Female Schizophrenics Suffering from Cyanosis and Hypotension.

In female schizophrenics who suffer from peripheral cyanosis and a low blood pressure, particularly in stuporous or restless patients, it was sometimes difficult to obtain a blood pressure reading by the usual method of auscultation at the elbow. When no sounds were audible a systolic reading had to be obtained by finding the pressure required to obliterate the radial pulse, this pressure being sometimes as low as 60 mm. Hg. More commonly one click was heard at the elbow, at a pressure a few millimetres higher than that needed to obliterate the radial pulse, or a sequence of a few beats was heard over a range of 2–10 mm. Hg. If the lowest pressure at which the brachial pulse is audible is taken to indicate the diastolic pressure, such readings as 100/96, 96/92 and 78/60 were recorded. The heart rate was usually slow in these patients, a rate of 56–64 per minute was common, and in the case of one patient who had a normal electrocardiogram, it was only 36 beats per minute. Palpation of the brachial arteries showed them to be unusually firm, of small calibre and easily rolled by the finger against the shaft of the humerus: pulsation was either absent, or was felt as a flutter in these contracted vessels. In the worst cases the brachial arteries were of the consistency and calibre of a quill, although none of the 28 patients who presented these vascular disturbances were over 35 years of age and the youngest was only 16. In a few instances the brachial vessel was soft and normal in the upper 2 or 3 in. of its course, where it could only be located by its pulsation, whereas below that level and down to the elbow it was firmly contracted, cordlike and pulseless. There could be no doubt that the palpated structure was the main vessel of the arm, as the radial pulse was obliterated by its compression and pulsation could be restored by immersing the arm (or an indifferent limb) in a bath of hot water. After vasodilatation had been secured by this means the brachial artery was perfectly normal in every case. The radial pulse was seldom absent, but it was frequently very small. The dorsalis pedis arteries of these patients were often pulseless, but they could be located as firm, narrow cords which could be rolled under the finger. Pulsation was frequently absent in the posterior tibial arteries at the ankle, but popliteal and femoral vessels were always normal.

The mean systolic blood pressure of 28 female schizophrenics who suffered from peripheral cyanosis and contracted brachial vessels was 93.5 mm. Hg $\pm$

1.8, their mean diastolic pressure 79.3 mm. Hg $\pm$ 2.5, and their mean pulse pressure 14.2 mm. Hg $\pm$ 1.92 (see Table XV).

TABLE XV.—*Blood-Pressure Readings of Female Schizophrenics with Contracted Brachial Arteries.*

Fem. pts. Number.	Mean syst. press. mm. Hg.	Mean diast. press. mm. Hg.	Mean pulse press. mm. Hg.
28	93.5 $\pm$ 1.80	79.3 $\pm$ 2.50	14.2 $\pm$ 1.92

A blood-pressure reading taken from the main artery of the arm, when this is firmly contracted, may not give reliable information about systolic and diastolic pressures above the level of vasoconstriction. It is, however, likely, in view of the low mean blood pressure of various groups of schizophrenics whose peripheral arteries showed no obvious abnormalities (and the small size of the heart and vascular tree of schizophrenic patients, to which attention is drawn later), that the low brachial blood pressure of these 28 schizophrenics was not merely the result of a localized change in the consistency of the wall of the brachial artery.

The retinal arteries of these patients appeared structurally normal, but they were often narrow and at times empty along short stretches of their course. The veins of the fundus were in most cases twice the diameter of the arteries, sometimes larger, but in a few cases they were also small in calibre and the fundus was then paler than usual. The retinal arteries did not dilate as readily as the limb vessels after reflex vasodilatation, but they dilated fully after inhalation, for 5 minutes or longer, of a mixture of carbon dioxide (30 vol.) and oxygen (70 vol.). Direct measurement of the diameter of the retinal vessels was attempted by projecting a micrometer scale on the retina, but the attempt was abandoned owing to the technical difficulties involved and the prolonged immobilization of the patient which it demanded. The impression was gained that the size of the retinal vessels of these patients was approximately normal during a mental remission. (A survey of the retinal appearances in 150 female and 50 male psychotics is reported later.)

Rise of Blood Pressure after Remission.

Twelve female schizophrenics who had a low initial brachial blood pressure showed a rise of blood pressure at the beginning of a remission, either spontaneous or following E.C.T. (see Table XVI).

In 6 cases the average blood pressure before a spontaneous remission was, systolic 89 mm. Hg $\pm$ 2.7, diastolic 73 mm. Hg $\pm$ 5.9, pulse pressure 16 mm. Hg $\pm$ 3.9; after the spontaneous remission the blood pressure of these patients was, systolic 120 mm. Hg $\pm$ 5.3, diastolic 85 mm. Hg $\pm$ 5.7, pulse pressure 35 mm. Hg $\pm$ 3.2. In another 6 cases the average blood pressure before remission was, systolic 99.5 mm. Hg $\pm$ 2.5, diastolic 85.1 mm. Hg $\pm$ 6.0, pulse pressure 14.3 mm. Hg $\pm$ 5.6; after remission following E.C.T. the blood pressure of these patients was, systolic 111.8 mm. Hg $\pm$ 2.4, diastolic 75.8 mm. Hg $\pm$ 3.9, pulse pressure 36 mm. Hg $\pm$ 2.3. The rise in systolic

TABLE XVI.—*Rise of Blood Pressure after Remission.*

Type of remission.	Number of pts.	Mean systolic pressure, mm. Hg.				Mean diastolic pressure, mm. Hg.				Mean pulse pressure, mm. Hg.			
		Before remiss.	After remiss.	Differ. of means.	Prob. level.	Before remiss.	After remiss.	Differ. of means.	Prob. level.	Before remiss.	After remiss.	Differ. of means.	Prob. level.
Spontaneous	6	89	120	31	<0.01	73	85	12	0.2	16	35	19	<0.01
		±2.7	±5.3	±5.9		±5.9	±5.7	±8.2		±3.9	±3.2	±1.7	
E.C.T.	6	99.5	111.8	12.3	0.01	85.1	75.8	9.3	0.2	14.3	36	21.7	0.01
		±2.5	±2.4	±3.5	-0.02	±6	±3.9	±7.2	-0.3	±5.6	±2.3	±6.1	-0.02
Total	12	94.25	115.9	21.65	<0.01	79.05	80.4	1.35	0.8	15.15	35.5	20.35	<0.01
		±2.3	±3.1	±3.9		±4	±4.5	±6.1	-0.9	±3.3	±1.9	±3.8	

TABLE XVII.—*Comparison of Mean Blood Pressure of Refractory and Socialized Patients.*

REFRACTORY PATIENTS.										SOCIALIZED PATIENTS.									
No. of pts.	Mean age years.	Mental illness.	Sys. press. mm. Hg.	Dias. press. mm. Hg.	Pulse press. mm. Hg.	No. of pts.	Mean age years.	Mental illness.	Sys. press. mm. Hg.	Dias. press. mm. Hg.	Pulse press. mm. Hg.	No. of pts.	Mean age years.	Mental illness.	Sys. press. mm. Hg.	Dias. press. mm. Hg.	Pulse press. mm. Hg.	No. of pts.	Mean age years.
46	38.2	Schiz. all varieties	118	75.8	42.2	32	45.8	Schiz. all varieties	131.5	83.3	58.2	32	45.8	Schiz. all varieties	131.5	83.3	58.2	32	45.8
	±1.57		±2.88	±1.64	±2.4		±1.87		±3.77	±2.73	±4.01		±1.87		±3.77	±2.73	±4.01		±1.87
32	32.2	Schiz. below 45	112.7	78	34.7	14	36	Schiz. below 45	127.7	85.4	42.3	14	36	Schiz. below 45	127.7	85.4	42.3	14	36
	±0.9		±2.5	±2.07	±2.33		±1.34		±5.9	±3.43	±1.5		±1.34		±5.9	±3.43	±1.5		±1.34
38	34.9	Schiz. excl. paranoics.	113.7	75.6	36.3	21	42.5	Schiz. excl. paranoics.	128.5	83	45.5	21	42.5	Schiz. excl. paranoics.	128.5	83	45.5	21	42.5
	±1.42		±2.74	±1.72	±2.77		±1.9		±4.67	±2.7	±4.5		±1.9		±4.67	±2.7	±4.5		±1.9
8	54.6	Paranoics	141.5	86.7	53.5	11	54.8	Paranoics	137	84.0	52.2	11	54.8	Paranoics	137	84.0	52.2	11	54.8
	±5.07		±5.8	±1.55	±6.45		±2.6		±6.15	±6.27	±7.18		±2.6		±6.15	±6.27	±7.18		±2.6
39	48.7	Non-schizophrenics	139	84	55	49	54.2	Non-schizophrenics	144	85	59	49	54.2	Non-schizophrenics	144	85	59	49	54.2
	±1.45		±2.77	±2.08	±3.12		±1.5		±3.47	±1.65	±3.07		±1.5		±3.47	±1.65	±3.07		±1.5

Difference of Means and Probability Levels.

Systolic pressure, mm. Hg.				Diastolic pressure, mm. Hg.				Pulse pressure, mm. Hg.			
13.5±4.8	<0.01	7.5±3.1	0.01-0.02	16.0±4.5	<0.01	0.01-0.02	4.5	13.5±4.8	<0.01	7.5±3.1	0.01-0.02
15.0±5.7	0.01-0.02	7.4±4	0.05-0.1	7.6±3.6	0.02-0.05	0.05-0.1	3.6	15.0±5.7	0.01-0.02	7.4±4	0.05-0.1
14.8±5.1	<0.01	7.4±3	0.01-0.02	9.2±5	0.05-0.1	0.05-0.1	5	14.8±5.1	<0.01	7.4±3	0.01-0.02
4.5±8.9	0.6-0.7	2.7±7.5	0.7-0.8	1.3±10.1	0.9	0.9	10.1	4.5±8.9	0.6-0.7	2.7±7.5	0.7-0.8
5.0±4.6	0.2-0.3	1.0±2.6	0.7	4.0±4.5	0.3-0.4	0.3-0.4	4.5	5.0±4.6	0.2-0.3	1.0±2.6	0.7

and pulse pressure is significant in both groups ; the change in diastolic pressure is not significant.

Average Blood Pressure of "Refractory" and "Socialized" Patients.

The lowest blood pressure readings in a survey of 550 female patients were almost invariably those of resistive, difficult schizophrenics.

The average blood pressure of female schizophrenics belonging to a so-called "refractory" ward was compared with that of female schizophrenics of a "socialized" ward (see Table XVII). There were 46 refractory schizophrenics, 38 catatonics and hebephrenics, and 8 paraphrenic and paranoid patients (here described as paranoids) in the refractory ward, also 23 hypomanics and 16 mental defectives and dementals whose history in many cases did not exclude a hebephrenic illness. There were 32 schizophrenics, including 11 "paranoid" patients in the socialized ward, also 20 affective psychotics and 29 mental defectives and dementals, several of whom were probably hebephrenics.

The average systolic pressure of 46 refractory schizophrenics was 118 mm. Hg $\pm$ 2.88, and that of the 32 socialized schizophrenics 131.5 mm. Hg $\pm$ 3.77, a significantly higher value for the latter ; the average systolic pressure of the 39 and 49 non-schizophrenic patients of these two wards was very nearly identical, 139 mm. Hg $\pm$ 2.77 and 144 mm. Hg $\pm$ 3.47 respectively. Seven of the 8 paranoids in the refractory ward had blood pressures well above the average for schizophrenic patients of this ward. These patients formed a small group apart, as they were not resistive and restless like the other refractory schizophrenics, but were dangerous and troublesome owing to their persecutory delusions. By excluding paranoids from the refractory and socialized groups, the average systolic pressure of these groups is lowered slightly, and is now 113.7 mm. Hg $\pm$ 2.74 for 38 refractory schizophrenics and 128.5 mm. Hg $\pm$ 4.67 for 21 socialized schizophrenics. It remains a significantly lower value for the former.

The average age of the socialized patients was slightly higher than that of the refractory patients, 45.8 years $\pm$ 1.87, compared with 38.2 years $\pm$ 1.57. If comparison is made of blood pressures of patients under 45 years belonging to these two wards, the average blood pressure of 32 refractory patients under 45, average age 32.2 years is, systolic 112.7 mm. Hg $\pm$ 2.5, diastolic 78 mm. Hg $\pm$ 2.07, pulse pressure 34.7 mm. Hg $\pm$ 2.33 ; of the 14 socialized patients under 45, average age 36 years, systolic 127.7 mm. Hg $\pm$ 5.9, diastolic 85.4 mm. Hg $\pm$ 3.43, pulse pressure 42.3 mm. Hg $\pm$ 1.50, a significantly lower systolic and pulse pressure for the former. There was no obvious reason why refractory schizophrenics should have a lower blood pressure, as their physical condition did not compare unfavourably with that of the patients in the socialized group ; only socialized depressives had, as a group, a noticeably poor physique compared to other patients in these two wards. There was no significant difference in the average blood pressure of the few paranoids or of non-schizophrenic patients belonging to the refractory and socialized wards.

Rise of Blood Pressure after Administration of Oral Sodium Chloride and of Intramuscular Desoxycorticosterone Acetate (Doca).

Sodium Chloride Additions to Diet.

The effect of sodium chloride additions to the ordinary diet was tried in the case of 3 young female schizophrenics who were suffering from increasing mental confusion and physical weakness. These patients had a low blood pressure but no other signs of Addison's disease. They were treated symptomatically by daily additions of 5 to 10 grammes of table salt to their ordinary diet and responded by a rise of blood pressure (see Table XVIII). In one case there was considerable mental improvement which initiated a good remission, while the blood pressure rose from 90/70 to 126/80 in 3 weeks. During the first week 5 g. salt was given daily, after this 5 g. on alternate days for 2 weeks. The second patient had a brachial systolic pressure of 70 mm. Hg before treatment was commenced, and only one sound was audible at the elbow on deflating the cuff; she received daily additions of 10 g. salt to her diet for 2 weeks and her blood pressure rose at the end of that time to 112/86, but fell to 80/76 5 days after treatment had to be abandoned, the patient refusing to take further salt additions, or sodium chloride cachets. In the third case the blood pressure rose from 90/70 to 110/70 after daily salt-additions of 5 g. for 4 weeks; there was some mental and physical improvement which enabled her to take part in ordinary ward activities.

Intramuscular Desoxycorticosterone Administration.

Five female schizophrenics, who had to be kept in bed owing to mental confusion and great physical weakness, had very low brachial blood pressures and were treated symptomatically with desoxycorticosterone acetate (Doca Organon, oil solution 2 mg. per ml.). (See Table XVIII.) Daily intramuscular injections of 5 ml. were given at the onset; after 2-3 days a rise of blood pressure was noted and the dosage was reduced to 3 ml. daily for one week, and then to 3 ml. on alternate days. Some physical improvement was evident in all 5 patients: in two of them, who had been almost *in extremis*, the change was remarkable. They became alert and instead of refusing food they were ravenously hungry, gaining several pounds in weight in a few days. Before treatment was commenced their respective blood pressure readings were 90/86, 98/90, 102/96, 90/70 and 80/70, and after this course of treatment their blood pressure had risen to 128/108, 115/85, 120/90, 118/90 and 100/70 respectively.

There was a definite improvement in the mental state of 2 of these 5 patients, one of whom proceeded to a spontaneous remission, another was discharged later after a course of insulin. They were both discharged "recovered" and there was no doubt in the mind of the observer and of the staff of the ward concerned, that doca had enabled these patients to survive at one stage of their illness. The other 3 patients showed little if any improvement and became more troublesome as they regained strength; they remained in fair physical health, their appetite having improved.

TABLE XVIII.—*Rise of Blood Pressure after Salt and after Doca Medication.*

Nature of treatment.	Number of pts.	Mean systolic pressure, mm. Hg.				Mean diastolic pressure, mm. Hg.				Mean pulse pressure, mm. Hg.			
		Before medication.	After medication.	Diff. of means.	Prob. level.	Before medication.	After medication.	Diff. of means.	Prob. level.	Before medication.	After medication.	Diff. of means.	Prob. level.
Salt added to diet 2-4 weeks	3	83.3 ±5.5	116 ±4.2	32.7 ±6.9	0.01— 0.02	70 ±3.9	78.7 ±3.9	8.7 ±3.9	0.1— 0.2	13.3 ±5.6	37.3 ±5.9	24 ±8.1	0.05
Doca parenterally 1-2 weeks	5	92 ±3.5	116.6 ±4.2	24.6 ±5.5	<0.01	82.4 ±4.8	88.6 ±5.5	6.4 ±7.3	0.4— 0.5	9.6 ±2.5	28 ±2	18.4 ±3.2	<0.01
All cases	8	87.7 ±3.3	116.3 ±3.1	28.6 ±4.5	<0.01	76.2 ±3.6	83.6 ±4.1	7.4 ±5.5	0.2	11.5 ±3.3	32.7 ±2.7	21.2 ±4.3	<0.01

Corticotrophin.

Injections of corticotrophin (Cortrophin kindly supplied by Organon, Ltd.) were given to 10 asthenic catatonic patients who had a low blood pressure. Five to 10 units, according to the severity of the case, were given intramuscularly on 14 consecutive days. There was no change in these patients' condition, apart from slight mental brightening and improved appetite in 3 cases after 20 units had been received.

Rate of Cutaneous Cooling and Vascular Responses to Cutaneous Stimuli of Schizophrenic and Affective Patients.

The comparative rate of cooling of two groups of female patients, schizophrenics and affective psychotics, after exposure of their limbs to different environmental temperatures, was investigated by measuring the fall in peripheral surface temperature over a given time. This fall is not a measure of total heat loss and results in part from adaptive peripheral vasoconstriction.

Reflex changes in the cutaneous blood supply, initiated by distal thermal or mechanical stimulation, were also investigated in these patients by noting changes in their peripheral surface temperature.

1.—*Comparative rate of cooling of schizophrenic and non-schizophrenic patients.*—Three groups of 6 to 9 schizophrenic patients observed at room temperatures 56° F., 66° F. and 70° F. were matched against an equal number of affective psychotics (see Table XIX). After resting for half an hour the

TABLE XIX.—*Relation of Environmental Temperature to Foot Temperature.*

Room temp.	Mental illness.	Pts. Number.	Mean foot temp. before exposure. °C.	Mean foot temp. after 1 hour's exp. °C.	Mean loss after 1 hour's exp. °C.
56° F. (13.3° C.)	Schizophr. Aff. psych.	6 6	22.3 ± 1.3 27.6 ± 2.02	18.75 ± 0.73 21.8 ± 0.8	3.55 ± 0.36 5.8 ± 0.89
66° F. (18.9° C.)	Schizophr. Aff. psych.	9 9	24.9 ± 1.72 26.73 ± 1.26	23.46 ± 0.82 25.9 ± 0.92	1.44 ± 0.83 0.83 ± 0.42
70° F. (21.1° C.)	Schizophr. Aff. psych.	8 8	25.2 ± 1.97 27.2 ± 1.38	24.25 ± 0.83 26.2 ± 1.04	0.95 ± 0.56 1.0 ± 0.34

patients were asked to sit quietly with bared feet for one hour longer. Their foot temperature was taken both before and after this period of time. The readings obtained gave no evidence of a quicker rate of cooling in the schizophrenic patients, who in every case had a lower initial and final average foot temperature than the corresponding affective patients. Affective psychotics had a higher average fall of surface temperature when they were exposed to the lowest room temperature, but their average final temperature remained higher than that of the schizophrenic patients.

2. *Immediate effect of a cold stimulus (immersing one hand in water 14.5° C.) on the foot temperature of schizophrenic and affective patients and of normal controls.*—Twelve schizophrenic patients were paired against 12 affective psychotics and 12 normal subjects (students) (see Table XX). Foot temper-

TABLE XX.—*Effect on Foot Temperature of Immersing One Hand for 3 Minutes in Water-Bath 14.5° C.*

Room temp.: 62° F. (16.7° C.).

Mental illness.	Pts. Number.	Mean initial foot temp. ° C.	Mean foot temp. aft. warming hand. ° C.	Mean gain or loss. ° C.
Schizophr.	12	18.91 ± 0.99	18.58 ± 1	-0.33 ± 0.08
Aff. psych.	12	24.58 ± 1.21	24.8 ± 1.16	+0.21 ± 0.13
Controls	12	24.5 ± 1.41	24.08 ± 1.4	-0.42 ± 0.18

Difference Between Means and Probability Level.

	Mean gain or loss. ° C.		Mean gain or loss. ° C.	Diff. betw. means. ° C.	Probability level.
Schizophr.	-0.33 ± 0.08	Aff. psych.	+0.21 ± 0.13	0.54 ± 0.15	<0.01
Schizophr.	-0.33 ± 0.08	Controls	-0.42 ± 0.18	0.09 ± 0.2	0.7
Aff. psych.	+0.21 ± 0.13	Controls	-0.42 ± 0.18	0.63 ± 0.22	<0.01

atures were recorded before and after immersing one hand in a bath of water 14.5° C., for 3 minutes. Eight of the schizophrenics showed a fall of 0.5–1° C., there was no change in 3 others and a rise of 0.5° C. in one patient. Five of the 12 affective psychotics showed rises of 0.5–1° C. and 7 showed no change. Eight normal subjects showed a fall of 0.5 to 1.5° C., 2 showed a rise of 0.5° C. and 2 no change. The average initial and final foot temperatures of the schizophrenic patients were again lower than those of persons in other groups and differed little in affective psychotics and normal subjects. The reaction of the schizophrenic patients to a thermal stimulus was similar to that of normal individuals and differed from that of affective psychotics, who showed more frequently a rise of foot temperature after cooling one hand.

3. *Tourniquet and cold water test.*—A tourniquet was applied to the arm of 6 schizophrenic patients, 6 affective psychotics and 6 normal subjects (students). Foot and hand temperatures were taken before and 3 minutes after suddenly raising the pressure in the arm-cuff well above systolic pressure (see Table XXI). Five of the 6 schizophrenic patients and all the normal subjects showed a fall of foot temperature, 0.5–2° C. in the former and 0.5–1° C. in the latter, but no change in the foot temperature of affective patients was recorded. There was a fall of temperature in the opposite hand in 4 schizophrenics and in 5 normal subjects, 0.5–3.5° C. in the former and 0.5–1° C. in the latter. No change was observed in the hand temperature of one schizophrenic; there was a fall in one and a rise in two of the 6 affective psychotics.

After arrest of the circulation the hand of each patient was placed in a bath of water 14.5° C. A further slight fall in foot temperature and a simultaneous rise in the temperature of the opposite hand now occurred in one schizophrenic; 2 normal subjects showed simultaneous falls of foot and hand temperature and 2 others a fall of foot temperature only. There was again no fall of foot temperature in affective patients, a slight gain in temperature of the opposite hand in 2 of them, a slight loss in another. Release of the pneumatic cuff while the hand remained immersed, caused further slight

TABLE XXI.—*Tourniquet and Cold Water Test.*

Room temp. 62° F. (15.6° C.).	Number of cases.	At onset.		Tourniquet applied to arm, 90 sec. reading.		Hand in water bath 14.5° C., 3 min. reading.		Tourniquet released while hand in water bath, 10 min. reading.	
		Mean foot temp. °C.	Mean hand temp. °C.	Mean foot temp. °C.	Mean hand temp. °C.	Mean foot temp. °C.	Mean hand temp. °C.	Mean foot temp. °C.	Mean hand temp. °C.
Schiz.	6	22.8 ±1.27	30.1 ±2.04	-0.91 ±0.31	-1.08 ±0.5	-1 ±0.38	-0.5 ±0.16	-1.25 ±0.29	-1.25 ±0.27
Affec.	6	23.08 ±1.73	30.66 ±1.7	0 ±0.02	+0.08 ±0.23	0 ±0.02	-0.08 ±0.39	-0.33 ±0.15	0 ±0.02
Controls	6	27.3 ±1.86	32.4 ±1.45	-0.58 ±0.06	-0.75 ±0.18	-1.08 ±0.2	-0.83 ±0.29	-1.16 ±0.41	-1.16 ±0.19

Difference of Means and Probability Levels.

	Mean loss of foot temp.		Diff. of means.	Prob. level.	Mean loss of hand temp.		Diff. of means.	Prob. level.
Schiz.	1.25 ±0.3	Affec. 0.33 ±0.15	0.92 ±0.34	0.02	Schiz. 1.25 ±0.27	Affec. 0 ±0.02	1.25 ±0.27	<0.01
Schiz.	1.25 ±0.3	Controls 2 ±0.42	0.75 ±0.52	0.2	Controls 1.25 ±0.27	Controls 1.16 ±0.19	0.09 ±0.33	0.7
Affec.	0.33 ±0.15	Controls 2 ±0.42	1.67 ±0.45	<0.01	Affec. 0 ±0.02	Controls 1.16 ±0.19	1.16 ±0.19	<0.01

falls of foot temperature in 2 schizophrenics and 5 normal subjects; a slight drop of $0.5-1^{\circ}$ C. was now noted for the first time in the foot temperature of 3 affective patients.

The average total loss of foot temperature for the schizophrenic patients was 1.25° C. ± 0.29 , for the normal subjects 2° C. ± 0.41 , and for the affective psychotics 0.33° C. ± 0.15 .

The reaction of schizophrenic patients to these mechanical and thermal stimuli was similar to that of normal persons, while affective psychotics showed little response to mechanical and cutaneous thermal stimuli and only a slight central vasoconstrictor response to chilled blood, after release of the tourniquet.

The schizophrenic patients differed from normal subjects and to a lesser extent from affective psychotics by their low initial and final peripheral temperatures.

These observations tend to show that exposure to the same environmental conditions does not cause a greater drop in the peripheral surface temperature of schizophrenic patients and no exaggerated response to mechanical and thermal stimuli when comparison is made with normal subjects under the same conditions of observation. They confirm, by addition of further examples, the low peripheral temperature of schizophrenic patients compared with affective patients (and in the present case compared with normal subjects) under the same environmental conditions. This tendency to a low peripheral temperature was noted throughout this study and showed only one exception: under conditions of high external temperature the average peripheral surface temperature of schizophrenics was no lower than that of affective psychotics under the same environmental conditions.

SUMMARY OF CLINICAL OBSERVATIONS.

(1) At room temperature $62-65^{\circ}$ F. ($16.7-18.3^{\circ}$ C.) cyanosis of the extremities, particularly of the feet, was present in 43 per cent. of 220 female and in only 5 per cent. of 300 male psychotics.

At room temperature 82° F. (27.8° C.) 246 female psychotics showed a similar high incidence of peripheral cyanosis. It occurred in 52 per cent. of the patients examined under these conditions.

Cyanosis was most common and most severe in female schizophrenics and mental defectives, several of whom were probably deteriorated schizophrenics. The highest incidence occurred in refractory (mainly catatonic) female schizophrenics.

Transient discoloration of the hands, unrelated to environmental temperature was a common occurrence in young schizophrenic patients of both sexes when they were observed under conditions of emotional stress during the early stages of their illness.

(2) At room temperature 62° F. (16.7° C.) the average surface temperature of the hands and feet of 30 female schizophrenics was significantly lower than that of 30 female affective psychotics.

The average surface temperature of cyanosed hands and feet of both male and female patients was significantly lower than that of the non-cyanosed extremities of these patients, but many individual exceptions occurred.

The average surface temperature of the hands and feet of 90 female psychotics was significantly lower than that of a similar group of 90 male psychotics; this difference vanished when comparison was made between average surface temperatures of (a) non-cyanosed extremities of male and female patients, and (b) cyanosed feet of male and female patients; the average surface temperature of the cyanosed hands of female patients was significantly lower than that of the cyanosed hands of male patients.

The average foot temperature of a group of female schizophrenics was the same as that of a similar group of female affective psychotics when these patients were examined at room temperature 75° F. (23.9° C.), but was significantly lower than that of the affective patients when the room temperature was only 60° F. (15.6° C.).

All the patients were examined after resting, with their limbs bared and under the same room conditions, but male patients wore heavier regulation clothing, both habitually and at the time of these observations.

(3) No correspondence between cyanosis of the extremities and advancing age was noted. Patients under 50 years of age were more frequently affected than those above this age.

(4) Imperfect correlation between cyanosis and inactivity was noted. While cyanosis was more frequent in patients who were inactive it was also present in some active workers and was absent in some patients who habitually adopted a standing position and who were examined after standing apparently immobile for several hours.

In some, but not all cases, cyanosis was less evident after strenuous physical exercise.

(5) The effect of posture on the circulation of cyanosed extremities is shown by diminution of cyanosis after raising the feet. This improvement was usually accompanied by an initial slight fall and a subsequent slight rise of average foot temperature, vasodilatation succeeding decongestion in this position of the limbs. Relief of cyanosis after raising the feet was more frequent in patients whose initial foot temperature had not been very low and in whom vasoconstriction had therefore not been excessive. In patients with a low foot temperature cyanosis often persisted after raising the feet, thermoregulatory vasoconstrictor responses remaining active after suppression of antigravity vasoconstrictor impulses.

(6) Temporary relief of cyanosis was afforded by any measure which secured vasodilatation, i.e. heating the body, reflex and reactive hyperaemia, and administration of a vasodilator drug. Local relief of cyanosis could also be secured by blocking the nerves of the limb.

Cyanosis of the extremities of 10 female psychotics, 5 schizophrenics and 5 depressives, improved simultaneously with the onset of a remission, which followed E.C.T., and recurred during mental relapse. Cyanosis was also relieved by the onset of spontaneous remissions (witnessed in 7 female schizophrenics) and by a course of insulin treatment.

(7) The brachial, radial, dorsalis pedis (and possibly the posterior tibial arteries) of 28 female schizophrenics who suffered from peripheral cyanosis were found on examination to be firmly contracted and pulseless, but these

vessels were normal after vasodilatation had been secured. Observation of the retinal vessels of schizophrenic patients suggested an even wider field of vasoconstriction.

The systolic and pulse pressures of 12 female schizophrenics who had contracted limb vessels were low; after a mental remission (spontaneous or following E.C.T.), significant rises of average systolic and pulse pressure, relief of vasoconstriction and clearing of peripheral cyanosis were noted.

(8) Comparison of average systolic and pulse pressures of 46 refractory female schizophrenics (average age 38.2 years) with those of 32 socialized female schizophrenics (average age 45.8 years) showed significantly higher values for the latter. Comparison of the average blood pressure of 32 refractory patients (average age 32.2 years) and 14 socialized female schizophrenics (average age 36 years) showed a significantly higher average systolic pressure in the latter. There was no significant difference in the average blood pressure of refractory and socialized paranoics of similar age groups, or of refractory and socialized non-schizophrenic patients, although the socialized patients belonged to an older age-group.

(9) Improvement in clinical condition and significant rises of average systolic and pulse pressures were observed in 8 asthenic female catatonics after oral administration of sodium chloride and after parenteral administration of doca.

(10) The rate of surface cooling of the extremities of schizophrenic and affective patients, observed at various environmental temperatures, showed no significant differences between these two groups.

In female schizophrenics and normal controls vasoconstrictor responses were easily elicited by distal thermal and other cutaneous stimulation, whereas vasodilator responses were more frequently elicited by similar stimuli in affective psychotics.

The schizophrenic patients differed from affective psychotics, and from normal controls, by their lower average peripheral surface temperature, both before and after cooling, and both before and after cutaneous stimulation.

REVIEW OF LITERATURE ON THE PERIPHERAL VASCULAR RESPONSES OF NORMAL AND PSYCHOTIC SUBJECTS.

Peripheral Vascular Responses of Normal Subjects.

Numerous studies of the peripheral vascular responses of normal and of cold-sensitive subjects have been communicated by Sir Thomas Lewis; they are summarized in part in Lewis' "Vascular Disorders of the Limbs" (6) and in three articles published by him in 1941 (7). Lewis described the cyanotic appearance of the extremities after exposure to chilly surroundings, which he attributed to a reduction of the cutaneous blood flow resulting from vasoconstriction. This reaction is augmented in some cases by an abnormal susceptibility to cold of the peripheral arterioles. The intensity of the discoloration and the fall in temperature vary with the degree of circulatory deprivation of the tissues, so that a violaceous colour corresponds to almost

complete arrest of the peripheral circulation. Passive congestion of the venules and of the subpapillary venous plexuses which give colour to the skin, follows slowing of the circulation and the consequent loss of tone in venules and capillaries; this is particularly noticeable when the limbs are dependent and is shown by deepening of the colour of the skin. While cooling of exposed surfaces occurs in most persons when the room temperature is lower than 64-68° F., the fall in temperature is modified by clothing and exercise. Contraction of the peripheral blood vessels in response to cold is due to three causes: the direct effect of cold on these vessels, transient general reflex vasoconstriction and more prolonged vasoconstriction resulting from increased activity of a tonic central mechanism. This central mechanism has been demonstrated by G. W. Pickering (8), who showed that if a limb is warmed after its circulation has been temporarily arrested (using the immersion method of J. H. Gibbon and E. M. Landis (9)), release of the tourniquet is followed by dilatation of the cutaneous vessels in the other 3 limbs; the warmed blood reaching the thermoregulatory centre lowers its vasomotor tone. Conversely, vasoconstrictor tone is raised when colder blood reaches the centre from the periphery.

Lewis' last articles were written at a time when injuries resulting from exposure to extreme climatic conditions and from immersion presented an urgent clinical problem. In these articles he demonstrates the identity of various tissue-reactions which follow excessive or prolonged cooling, chilblains, erythrocyanosis and trench-foot, and shows them to be either subacute or chronic inflammatory lesions. In cold-sensitive persons, whose vasoconstrictor responses are unusually brisk, local injuries may follow moderate chilling. They may predispose to further injuries which become progressively more severe, a vicious circle due to increased vulnerability of previously-damaged tissues.

The frequent limitation of cyanotic disturbances to the hands and feet is shown by Lewis to depend on the part played by the extremities in the heat-regulating mechanisms of the body. Their efficiency as radiators is due to their anatomical configuration and to their abundant subcutaneous blood supply; it is enhanced by numerous arteriolo-venous anastomoses described by R. T. Grant (10). These anastomoses have a rich vasomotor supply and they act as sluices permitting rapid shunting to and from the skin of a considerable proportion of the blood which reaches the extremities; they protect local tissues and prevent loss of body-heat. In excessive thermoregulatory reactions the extremities may suffer if their blood supply is lowered below the minimum requirements of the peripheral tissues.

Many observers have noted the preponderance and persistence of vasoconstrictor impulses to the vessels of the lower extremities (G. W. Pickering (8), J. Doupé, J. S. M. Robertson and E. A. Carmichael (11), etc.). The added flow of antigravity impulses, which are necessary for the maintenance of an efficient systemic circulation, may lead to excessive cutaneous reactions during exposure to extreme cold, and the high incidence of cyanotic disturbances of the feet is partly explained by the presence of this second vasoconstrictor mechanism.

A protective local vasodilator reflex, described by Lewis, is normally evoked by minor tissue injuries; it is less effective when the tone of the vessels is high and may fail in cold-sensitive persons in whom this physiological adjustment would be particularly valuable.

The course of the sympathetic fibres to the peripheral vessels was described by T. Lewis and G. W. Pickering (12), who demonstrated vasoconstrictor fibres in the main nerves of the limbs; these fibres are distributed with the sensory supply to the skin and can be traced by blocking a nerve with a local anaesthetic, or by mapping the vasomotor loss in accidentally denervated skin (J. R. Learmonth (13)). Vasodilator fibres to the vessels of the hand have been demonstrated by T. Lewis and G. W. Pickering (12) and those supplying the lower extremities by T. J. Fatheree (14); however, all these observers agree on the relative unimportance of vasodilator impulses compared with the active control of the vessels by vasoconstrictor nerves.

V. Uprus, J. B. Gaylor and E. A. Carmichael (15) have shown that the time of onset of active vasodilatation depends on local conditions, the temperature of the tissues, the position of the limb and the rapidity with which the blood temperature is raised. R. Jung and E. A. Carmichael (16) insist on the necessity of relating these vascular reactions to the pre-existing condition of the vessels, as many erroneous statements which claim to describe failure of vascular responses in psychotic patients have been based solely on a disregard of this elementary precaution.

Peripheral Vascular Responses of Psychotic Subjects.

The peripheral vascular reactions of psychotics were studied by D. I. Abramson, who summarized his researches, extending over a number of years, in his book, *Vascular Responses in the Extremities of Man in Health and Disease* (17). With a venous occlusion plethysmograph, Abramson was able to demonstrate a tendency to diminished blood flow in the hands of psychotic patients, due to a neurogenic reduction of the calibre of the vessels. Excessive vasoconstriction was abolished after local or reflex warming which resulted in full vasodilatation, proving the absence of organic lesions of the vascular tree. Vasoconstrictor responses could be elicited in both psychotic and normal subjects by painful cutaneous stimuli, exercises in mental arithmetic, or inhalation of mixtures of air and carbon dioxide. Abramson considers that increased tone of the vessels of the hand in schizophrenic patients, and the ensuing stasis in the veins of the forearm, account for the supposed slowing of the systemic circulation reported by observers who have used these veins in their experiments. He noted a temporary improvement in the circulation of the hand, forearm and leg during the height of insulin-hypoglycaemia, and a more permanent improvement in some schizophrenic subjects after a course of insulin comas.

The vasomotor disturbances of a group of akinetic catatonics were studied by R. Jung and E. A. Carmichael (16). In agreement with D. E. Cameron (18) these authors found that heat-production was low and heat-regulation was active in these patients. The cyanotic disturbances which they observed were attributed by them to immobility, immobilization of a limb always

resulting in a fall of surface temperature. They suggest that the simultaneous clearing of vasospasm and stupor, reported by P. Tomescu (19), may have been a result of increased bodily activity which coincided with the end of stupor. They found no evidence in their patients of the failure of vasoconstrictor reactions, or of unresponsiveness to adrenaline; reported failure of these reactions is due to the inability of initially contracted vessels to respond "normally" to further vasoconstrictor stimuli; conversely, adequate means for securing vasodilatation are necessary when we are dealing with fully-contracted vessels.

The effects of emotional disturbances on the peripheral circulation and skin temperature were studied by B. Mittelman and H. G. Wolff (20). These observers noted a fall in the finger temperature, which was most marked when frustration was revealed by psychoanalysis, and was also present in states of depression, anxiety, fear or conflict, but was usually absent when security had been achieved, by repression, detachment, or even by reassurance. Vasospasm of the digits is relieved during treatment by suggestion, according to M. Lipkin and his co-workers (21); J. Mufson (22) showed that vasoconstrictor responses initiated by fear were sufficiently pronounced in cases of Raynaud's disease, to obliterate the narrowed digital vessels and were as effective in this respect as local applications of cold. L. A. Gottschalk (23) observed the conditioned vascular reactions of normal subjects (students) and found that they were facilitated by a pre-existing imbalance of the autonomic nervous system. The consensus of opinion of these various observers emphasizes the importance of emotional factors in initiating, or enhancing, a peripheral vascular reaction.

Vasomotor instability in schizophrenic patients was studied by L. Minski (24); he described the almost constant occurrence of cyanotic disturbances in stuporous patients who suffered from occasional vasovagal attacks. Since massage and passive movement did not relieve cyanosis, this observer does not believe it to result from a lack of exercise; it was unrelated to the level of the systemic blood pressure but was clearly related to chilling. E. S. Stern (25) also studied cyanotic disturbances in an asylum population. He observed that clearing of cyanosis occurred during periods of increased bodily activity and in warmer weather and attributed the vascular disturbance to the effects of cold and inactivity on the peripheral circulation. In severe cases of cyanosis prolonged bed rest was necessary to restore the limbs to their normal appearance. Stern found no difference in the incidence of cyanosis in male and female patients, but his description indicates that woollen hose was worn by patients of both sexes. Greater proneness of female patients to somewhat similar disturbances of the peripheral circulation was noted by Lewis (6), who called erythrocyanosis "a malady of women," and attributed its occurrence to the lighter clothing worn by women. Lewis noted that changes in the cutaneous distribution of cyanosis followed changes of fashion, the wearing of shorter skirts or of silk stockings. F. Layani (26) also found a preponderance of women among patients suffering from acrocyanosis and attributed this defect to a diminution of vascular tone in women, or to possible ovarian dysfunction.

In biopsies of skin taken from the dorsum of the hand of patients who showed peripheral cyanosis, E. S. Stern (25) has noted thickening of the medial coat of the arterioles, a true hypertrophy resulting from prolonged vasoconstriction.

Contraction of the larger peripheral vessels has been observed by G. K. Stürup (27). He reported a case of psychogenic shock which terminated fatally in a young schizophrenic woman. After a severe fright this patient collapsed; her radial arteries were so firmly contracted that they did not bleed when they were severed for an attempted transfusion. Stürup believes contraction of the peripheral vessels to be a feature common to psychogenic and traumatic shock. Other observers have paid little attention to the condition of the main limb vessels of psychotic patients and these are rarely mentioned in clinical descriptions of peripheral cyanosis. T. Lewis (28) observed a contracted radial artery, to which he attached little importance, in a patient who suffered from a Raynaud-like syndrome. On several occasions, however, Lewis states that all the vessels of the limb participate in vasoconstrictor responses evoked by chilling (29). D. M. Blair, F. Davies and W. McKissock (30) and E. D. Telford and J. S. B. Stopford (31), who were interested in the changes which occur in patients suffering from a cervical rib syndrome, have remarked on the occasional difference in calibre of the axillary and brachial arteries of these patients, the former vessel being normal, the latter sometimes pulseless and cord-like. This difference is attributed to vasoconstriction of the brachial artery, resulting from pressure on its sympathetic supply at the level of the first rib (or cervical rib). The subclavian and axillary arteries, which are supplied directly from the sympathetic chain, are not affected. In a plethysmographic investigation of patients who suffered from dementia praecox, H. de Jong (32) found evidence of lasting vasoconstriction, a "Spannungszustand" or "Volumstarre" of the peripheral vessels. P. Tomescu (19) has also observed permanent vasoconstriction in the vessels of catatonic patients. More recently T. Klingman (33) stated that he had found spastic contraction of the radial arteries in almost every schizophrenic patient he examined; this contraction persisted in a hot room but was relieved with the onset of mental improvement. He attributes the spastic condition of these vessels to depression of the autonomic centres, an explanation which is difficult to follow, as vasoconstriction is a sign of sympathetic overactivity rather than of its failure.

Several authors have noted the importance of genetic and personality factors in the aetiology of excessive vasoconstriction. W. Block (34) has reported a study of German soldiers on the Russian front, which led him to conclude that individual susceptibility (vasomotor constitution of the individual) was second only to exposure as a factor determining the occurrence of frost-bite. Asthenic subjects were found to be much more prone to these injuries than pyknic subjects, and 50 per cent. of the patients who had to be invalided with frost-bite were known to have suffered habitually from cold extremities. J. R. Learmonth (35) speaks of an hereditary type of cold fingers when referring to patients whose fingers have been cold and cyanosed since childhood. H. Jost and L. W. Sontag (36) found support for a genetic

theory of autonomic dysfunction in the significantly greater similarity of the results of tests of autonomic function, vasoconstrictor response, conductance, pulse pressure, etc., in monozygotic twins, compared with those of siblings and unrelated persons. They therefore concluded that genetic factors may determine a predisposition to psychosomatic illness.

W. Linford Rees (37) has reported a greater incidence of schizoid traits in leptomorphs than in mesomorphs or eurymorphs. His observations support Kretschmer's classification, but he found the percentage of eurymorphs in the schizophrenic group to be higher than that indicated by Kretschmer. Rees considers that the physical aspect of human constitution is more than an incidental factor, not only in determining susceptibility to a psychosis, but also in influencing the form and progress of the illness.

Conclusions.

When the vascular disturbances of the patients examined in this hospital are reviewed in relation to the work of other observers, the following conclusions appear to be justified.

Peripheral Vascular Disturbances.

The vascular disturbances of these patients closely resemble those observed by Lewis and his co-workers in normal persons exposed to cold surroundings; they differ from them only in the ease with which they are elicited at ordinary room temperature and by their intensity and chronicity. Vasoconstriction of the extremities was very severe in some of these mental patients, particularly in schizophrenic women, whose hands and feet showed signs of excessive reduction of the circulation, chronic cyanosis, atrophy or thickening of the skin, oedema, stasis and superficial ulceration. These appearances are identical with those which were noted in "cold-sensitive persons" by Lewis and other observers, and with those which occur in normal persons subjected to severe or prolonged exposure.

It has long been recognized that schizophrenics and mental defectives are particularly prone to peripheral cyanosis, the greater frequency of its occurrence in female patients, which was noted in the present series being, however, exceptional. Female patients of this hospital wore lighter clothing than male patients, and either no stockings or cotton stockings which were frequently discarded. It is noteworthy that woollen stockings were worn by female psychotics who showed no higher incidence of cyanosis than the male psychotics of the same institution (E. S. Stern (25)). The clothes worn by female patients were of poor quality under war and post-war conditions, whereas the suits worn by the male patients were made of heavy material. These differences had added importance while restrictions in the use of fuel were still enforced, and there was little doubt in the mind of the observer that chilling was the main cause of cyanosis among female patients. Complaints of "feeling cold" were, however, exceptional, and complete indifference to chilling was the rule. These patients often sat under an open window instead of taking an available chair by the fire.

In mental patients slight chilling was sufficient to induce severe cutaneous reactions, a marked increase in the number of cyanosed male patients being observed after exposure of their bared limbs for half an hour to ordinary room temperature. Other factors, apart from chilling, which may have contributed to a higher incidence of cyanosis in female patients, such as metabolic and endocrine differences between the sexes and differences in the degree of activity of male and female patients, are considered later under the appropriate references to the literature.

Relation of Cyanosis to Bodily Activity.

Cyanosis of the extremities could not always be related to inactivity. Although it was more common in inactive subjects, as might be expected if it reflected the need for conserving body heat, it was sometimes severe in extremely restless patients and was not always alleviated by physical exercise. Its presence in restless patients, and its invariable absence in those who performed useful tasks, are proof that inactivity is not its main or only cause. Clearing of cyanosis was frequently observed during a mental remission, even when this was associated with decreased restlessness. R. Day and W. O. Klingman (38) and D. I. Abramson (17), etc., have reported the relief of cyanosis during sleep. Their observations were confirmed in several patients observed at this hospital, although relief of cyanosis was not always complete. This improvement may have been due to greater warmth or to diminished mental and bodily tension, but it cannot be attributed to increased bodily activity.

Emotional Vascular Responses.

Fleeting cyanotic discoloration of the hands of young schizophrenic patients of both sexes, dependent on emotional stresses rather than on chilling, is probably akin to the "emotional circulatory disturbance" described by Abramson (17), Mittelman and Wolff (20), Mufson (22), etc., a psychogenic vasoconstrictor response occurring in an emotionally unstable person.

Conditioned responses were not investigated here. It seems likely that they play their part in recurring vasoconstrictor reactions, the emotional experience which accompanies or precipitates a first excessive reaction serving as a conditioned stimulus for second and subsequent reactions, which may be progressively more severe, as noted by Lewis (7).

Vasoconstriction of Large Vessels.

Extreme contraction of the peripheral arteries and consequent absence of pulsation in large vessels were striking physical signs in some of the schizophrenic patients examined here. It is possible for an absent pulse to indicate only an abnormality in the course of a limb vessel, a fact pointed out by H. Morrison (39), but in these mental patients the contracted pulseless vessels are easily palpable as firm, cord-like structures, which are restored to their normal condition after vasodilatation and then pulsate vigorously. Contraction of the larger limb arteries may be interpreted as part of a protective

thermoregulatory mechanism which is responsible for peripheral vasoconstriction and cyanosis, an excessive reaction initiated by the urgent necessity of conserving body heat. A reduction of the total blood volume may have been present in some of these cases; this is suggested by a few observations reported in the literature, but no reliable estimations are yet available and a blood-shift may be an alternative explanation for a low brachial blood pressure, under conditions of extreme peripheral vasoconstriction. Contraction of the brachial artery in the presence of normal subclavian and axillary vessels has been attributed in the case of patients suffering from a cervical rib syndrome to irritation of the sympathetic fibres supplying the brachial artery (Blair and Davies (30), Telford and Stopford (31)). In mental patients who do not suffer from a cervical rib syndrome, this contraction, relieved by both direct and indirect warming, must be regarded as part of an exaggerated heat conserving reaction, in which all "peripheral vessels" participate. The axillary artery is not a "peripheral vessel" in this sense, a physiological distinction between the proximal and distal parts of the main artery of the arm being revealed by this difference.

The relief of vasoconstriction which accompanies a mental remission coincides with a rise of brachial blood pressure and with simultaneous relief of peripheral cyanosis. These physiological reactions are difficult to explain, but they are elucidated by the work of W. Machle and T. F. Hatch (40). These two observers have concluded, from their careful review of man's thermal relation to his surroundings, that man's performance under various environmental conditions is a measurable quantity which is qualitatively different from measurable differences of isolated components of the reaction. This observation is particularly apt when the thermal reactions of psychotics are considered. Their maladaptation, as judged by a poor physical performance, may in reality be an adaptation to a situation not envisaged by the observer. Increased bodily activity, for instance, is a "normal" response whenever the body temperature is lowered, but is out of place when chilling accompanies sleep and catatonic stupor, or hibernation in animals. Only vasoconstriction remains to diminish heat loss in catatonic patients. Diminished responsiveness to the environment is common to sleep, catatonia and hibernation; cooling is permitted as a necessary accompaniment of the lowered metabolic level while the body recuperates during sleep; a lowered metabolic rate during hibernation may assure survival of an animal by conserving his dwindling food-stores. It is now suggested that a lowered metabolic rate may be a necessary accompaniment or a possible prerequisite of catatonic withdrawal, permitting a retreat from a situation which is intolerable. It is interesting to note in this respect that chilling, which is considered a result of hibernation, may also be its cause, as was observed by I. Ariel, F. W. Bishop and S. L. Warren (41).

No genetic investigation or typological classification has been attempted here. If the reputed preponderance of asthenic, leptosomatic types in catatonic schizophrenics is accepted, their liability to cyanosis may rest on a constitutional basis. The general clinical impression suggested a greater frequency of leptosome type in catatonics and hebephrenics, and of pyknic

body-build in paranoid patients. This clinical impression, for what it is worth, receives support from the studies of B. J. Betz (42), C. J. Conolly (43) and others, who have commented on differences in the typology of these two schizophrenic sub-groups. Evidently the question can only be settled by observing the relative permanence of clear-cut catatonic and paranoid syndromes in patients with pronounced typological differences. The fluidity of the two syndromes and their successive occurrence in the same patient appear, at first sight, unfavourable to the theory of their genetic predetermination.

THE CARDIOVASCULAR APPARATUS, BLOOD PRESSURE AND BLOOD VOLUME OF SCHIZOPHRENIC PATIENTS.

Post Mortem Appearances.

Nolan Lewis (44) has studied the post mortem appearance of the cardiovascular system of 600 cases of dementia praecox. In hebephrenics and catatonics he found that the size of the heart was invariably smaller than normal and the aorta was also frequently smaller than normal. Paranoid cases showed fewer vascular abnormalities than other schizophrenics. Hypertrophy of the heart was never observed, even in cases with valvular lesions. The vessels of the brain were reduced in size and their perivascular spaces were correspondingly enlarged. This striking vascular aplasia was attributed by Lewis to an early arrest of development and to failure of the normal response to increasing demands on the vascular system during growth of the body.

Capillary Structure.

Numerous studies on the structure of peripheral capillaries in psychotic patients have been published and some observers have attributed diagnostic or aetiological significance to changes in capillary pattern. D. M. Olkon (45), who studied the defects of capillary structure in 1,047 schizophrenics, considered them to be related to the severity of the psychosis. He found that the capillaries of the web of the fingers were reduced in number and that they were stellate, spiral or crescent-shaped. Since these changes usually persisted after a mental remission, although normal comma-shapes were then more numerous, Olkon regarded them as permanent structural defects. Similar changes have been described by S. Cobb, M. E. Cohen and D. W. Badal (46) in 53 per cent. of the patients suffering from neurocirculatory asthenia and in 21 per cent. of their normal controls. E. Davis (47) also found a similar disturbance of capillary pattern in patients suffering from Raynaud's disease, or from other forms of vasomotor instability. A. Hauptmann (48) reported abnormal capillary patterns in 88 per cent. of his patients with a "neurotic" constitution and 7 per cent. of the normal subjects examined by him, but in 4 per cent. only of the patients with a "neurotic reaction." All these observers have used the skin of the nail fold or that of the web of the fingers for their examination, and it seems possible that the capillary changes they observed were related to peripheral vasoconstriction and passive venous congestion

which are frequently present in patients belonging to the groups they investigated. This supposition is strengthened by the description given by R. Greene (49) of changes in the capillaries of the skin adjoining a shallow gangrenous lesion on the finger of a patient suffering from anorexia nervosa, peripheral vascular spasm and a low basal metabolic rate.

Systemic Blood Pressure.

R. G. Hoskins and E. M. Jellinek (50) consider that the average systolic pressure of schizophrenic patients is about 87 per cent. and their average diastolic pressure about 85 per cent. of the normal value. G. Steiner and A. Strauss (51) have noted a low blood pressure and pulse pressure in dementia praecox patients. In an early publication O. Pförtner (52) reported a low systolic blood pressure of approximately 95 mm. Hg in praecox patients who suffered from cold, cyanosed extremities. H. Freeman, R. G. Hoskins and F. H. Sleeper (53) have published a comparative study of the blood pressure of first-year students and of 180 male schizophrenics. They found an average blood pressure of 115/71 mm. Hg in the former and of only 104/54 mm. Hg in the latter. The highest readings were those of paranoid patients, the lowest those of catatonics. These observers failed to find any correlation between the blood pressure and the body weight. They considered that vagotonic bradycardia and diminished vasoconstrictor tone were partly responsible for the low blood pressure of these patients, a surprising conclusion in view of the notorious tendency to peripheral vasoconstriction shown by schizophrenics. J. C. Rheingold (54) has compared the mean blood pressure of 129 male and female schizophrenics, in an early stage of their illness, to that of the general population (life insurance applicants) and has found a lower systolic and diastolic value and considerably lower pulse pressure for the schizophrenic group.

The peripheral venous pressure of schizophrenic patients was measured by C. M. Krinsky and J. S. Gottlieb (55), who found it to lie within normal limits even when severe peripheral cyanosis was present; their observations exclude the possibility of venous obstruction as a cause of these peripheral vascular disturbances, a conclusion previously reached by T. Lewis. D. E. Cameron and E. M. Jellinek (56) observed a rise in the systolic pressure of schizophrenic patients who had responded to insulin treatment, and they noted that patients who subsequently recovered had a lower blood pressure before treatment than others who later derived no benefit from a course of insulin comas. In a radiological study of the heart of schizophrenic patients, M. J. Farrell and E. Vassaf (57) were able to demonstrate that the heart increased in size after successful insulin treatment, and diminished in size during a mental relapse.

J. S. Gottlieb (58) has commented on the high correlation between the systolic and diastolic blood pressure of schizophrenic psychotics, which he ascribed to the relatively static vascular bed of these patients and to their diminished responsiveness to sympathetic stimulation. Like R. G. Hoskins and E. M. Jellinek, he believes that a high correlation of systolic and diastolic

blood pressure in schizophrenia indicates a physical approach to a stable hydrodynamic system. (Vascular rigidity, or static conditions of the vascular bed of schizophrenic subjects are frequently mentioned in the literature, often without reference to vasoconstriction as their only known cause.)

Blood Volume.

J. M. Looney and H. Freeman (59) compared the blood volume of 870 schizophrenic patients and 29 normal males, by the Congo red method of Rowntree. They found a normal average value for the blood volume of the former, compared with body weight, but a low value compared with body surface, only 2,824 c.c., instead of the normal average value of 3,007 c.c. per square metre body surface. The reason for the discrepancy between these two measurements remains unexplained, but comparison of blood volume with body surface, rather than body weight, is favoured by Hoskins and his school. I. Finkelman and D. Haffron (60) also used the dye method for their blood volume estimations. They found evidence of a diminished volume of circulating blood in 39 dementia praecox patients, compared with that of 15 manic-depressive subjects, i.e. 2,609 c.c., instead of 2,973 c.c. per square metre body surface; this latter figure is regarded as an approximately normal value. (No report of recent investigations, undertaken with modern methods of blood volume estimation, was found in the literature and the question of a possible decrease in blood volume in some variety or stage of schizophrenic illness must await future investigation.)

Retinal Blood Vessels and Blood Pressure.

A study of retinal blood vessels is reported by J. M. Cotton, N. D. C. Lewis and A. W. Egenhofer (61). These workers estimated the capacity of the arterial vascular bed in two groups of patients, schizophrenics and manic-depressives, by measuring with the eye-piece of a Gullstrand ophthalmoscope the diameter of all the arterial branches at the edge of the optic disc. They found no correlation between the estimated capacity of the retinal bed and the two psychoses investigated, nor with the patients' type of body build, but found a high correlation with the clinical status of schizophrenic patients; those who were deteriorating, or who had failed to improve under treatment, had significantly smaller vascular beds than others who were improving at the time. F. Morel, A. Franceschetti and E. B. Streiff (62) agree with Freeman, Hoskins and Sleeper (53) that low systemic blood pressures are common in dementia praecox. In a study of retinal blood pressures in 60 of these patients they found a greater than average number of retinal hypotensives and a smaller than average number of retinal hypertensives; the retinal blood pressure showed, on the whole, a good correlation with the systemic blood pressure, but was sometimes lower than predicted. In another group, consisting of 48 paranoid ("chronic hallucinatory") psychotics, these observers found no significant differences from average retinal blood pressures, while the systemic blood pressure was often raised.

Angiospastic retinopathy is the subject of several recent communications. These are reviewed by M. A. Zeligs (63) who states that vasoconstriction, resulting from fear or from anxiety, in patients who show a tendency to sympathetic overactivity, is the main cause of this condition, retinal vasoconstriction being merely a focal manifestation of a general vasospastic state which involves the peripheral vessels. S. R. Gifford and G. Marquardt (64) also observed peripheral vascular disturbances, acrocyanosis and arteriolar spasm in patients who suffered from angiospastic retinopathy, and noted that these attacks could be precipitated by chilling or by psychogenic causes.

Vasoconstriction of the retinal arteries during attacks of migraine has been reported by several workers: E. Bramwell (65) observed its occurrence, usually followed by vasodilatation, before the onset of an attack. S. Cobb believes that emotion plays a part in precipitating these attacks, concurrent vasomotor changes being responsible for paling and flushing of the cerebral cortex. In an article published with W. G. Lennox (66) he noted the ipsilateral diminution of the calibre of the smaller cerebral arteries which follows experimental stimulation of the cervical sympathetic. When discussing hypertensive cerebral attacks, D. McAlpine (67) referred to the occurrence of minor cerebral symptoms which clearly pointed to the existence of cerebral angiospasm. Disturbances of vision were usually transient, vision being affected in some cases independently of retinitis, by the spasm of a branch of the posterior cerebral artery. Corroborative objective evidence of the importance of cerebral vasoconstrictor impulses is furnished by the occurrence of cerebral vasodilatation after cervical sympathectomy, which has recently been demonstrated by arteriography (68).

E. Guttmann (69) considered that although no direct proof of the correlation of peripheral vascular disturbances with cerebral vascular changes is yet available, the adoption of this hypothesis is justified by numerous reports of the coincidence of confusional states with attacks of Raynaud's disease.

The Vasodilator Effect of Carbon Dioxide.

The dilator effect of carbon dioxide on cerebral and retinal blood vessels has been noted by many observers. S. Cobb and F. Fremont-Smith (70) described the arterialization of retinal veins a few minutes after the inhalation of a mixture of 10 per cent. carbon dioxide in oxygen. They compared this "dramatic change" with changes observed by H. G. Wolff and W. G. Lennox (71) in cerebral vessels, namely, dilatation of the capillaries and increased volume of flow. A. S. Loevenhart, W. F. Lorenz and R. M. Waters (72) reported a striking mental improvement in stuporous catatonics, depressives and involutional melancholics after inhalation of mixtures of carbon dioxide and oxygen. These authors noted mental changes similar to those observed by them after intravenous administration of sodium cyanide: Catatonic patients were aroused from stupor and became accessible; they moved about freely and were generally willing to speak, but they relapsed after 2 to 25 minutes, either suddenly or gradually, and reverted to their previous condition, resuming their customary postures. Cinematographic evidence

of the temporary improvement which follows carbon dioxide inhalation is presented by H. C. Solomon, M. R. Kaufman and F. C. D'Elseaux (73). A striking change was shown in the appearance and demeanour of catatonic patients who had a Parkinsonian gait and expression before inhalation. They regained a normal expression and gait, but relapsed a few minutes later, assuming typical catatonic postures.

Intracranial Blood Flow.

Estimations of the total intracranial blood flow in man must be based on indirect methods of calculation; the displacement of the cerebrospinal fluid after temporary blocking of the internal jugular veins (E. B. Ferris (74)), or comparison of the oxygen content of arterial and jugular blood (W. G. Lennox and E. L. Gibbs (75)) are the methods which have been found most reliable for calculating the total cerebral blood flow. The first method is said to give an index of a function of the total intracranial circulation; it is open to serious criticism, on both physiological and physical grounds, as the cranium cannot be considered a "closed box." The second method is only accurate if the metabolic requirements of the brain are assumed to be constant and this assumption has been disproved, at any rate in the case of hypoglycaemic metabolism. Diminished arterio-venous oxygen differences during coma, observed in man by H. E. Himwich, K. M. Bowman, J. Wortis and J. F. Fazekas (76) result from lowered utilization of oxygen and not from an increased cerebral blood flow; the volume of circulating cerebral blood is actually diminished during hypoglycaemia, according to J. Loman and A. Mayerson (77) who measured the flow by a thermo-electric needle inserted into the jugular vein, a method devised by F. A. Gibbs (78). Another, and possibly more promising method of calculating the total cerebral blood flow in man has been introduced by S. S. Kety and C. F. Schmidt (79). It is based on estimations of the arterial and internal jugular blood concentration of an inert gas, nitrous oxide, during the first ten minutes of its inhalation in low concentration. A simultaneous but separate estimation of the arterio-venous oxygen difference is used as a measure of cerebral metabolism. Schmidt's method requires complex mathematical adjustments, which are designed to exclude numerous physiological and physical fallacies. These corrections arouse the suspicion that unknown fallacies may have been overlooked, but experienced workers, such as W. A. Himwich, E. Homburger, R. Maresca and H. E. Himwich (80) consider this method reliable; parallel experiments involving direct estimations of the total blood flow in experimental animals appear to confirm this view. Separate estimations by these authors of the concentration of nitrous oxide in the blood of both jugular veins gave some indication of the respective metabolic requirements of the human cortex and of the basal structures of the brain. The oxygen consumption of the former is stated to be 3.9 c.c. per 100 g. tissue per minute and that of the structures drained by the opposite jugular vein only 2.7 c.c. per 100 g. tissue per minute.*

* Kety and Schmidt question the validity of these conclusions in their latest publication (*J. Clin. Invest.*, 27, 476, 1948). They found no significant difference between the blood flow and oxygen consumption calculated from right and left jugular blood.

The conclusions drawn by these observers from their elaborate experiments support the view expressed by earlier workers, namely, that the volume of cerebral flow is partly determined by metabolic requirements of the brain, and that both the metabolic requirements and the flow are diminished during anaesthesia.

As the present methods of estimating the cerebral blood flow can only yield gross approximate values it is surprising to find a considerable measure of agreement between various observers. No change from average normal values has been claimed for psychotic subjects who do not suffer from an "organic" psychoses. An apparent exception to this rule is reported by M. Rosenbaum, E. Roseman, C. D. Aring and E. B. Ferris (81), who found a smaller average value in 16 schizophrenics compared with 18 non-psychotics, but wide scatter from person to person in the schizophrenic group led them to conclude that this diminution was not significant. These workers failed to find any correlation between the volume of the cerebral blood flow and the type of schizophrenic illness from which the patients suffered, but some correlation seemed likely between the volume of flow and the degree of psychomotor activity displayed by the patients. H. E. Himwich, K. M. Bowman, J. Wortis and J. F. Fazekas (76) used arterio-venous oxygen differences for the estimation of cerebral metabolism and found a normal average value (with wide scatter) for 11 schizophrenics, which they interpreted as evidence of a normal cerebral metabolic rate. Normal metabolic values were also reported by J. Wortis, K. M. Bowman and W. Goldfarb (82) who used the same method for estimating the cerebral metabolism of schizophrenic patients, both before and after insulin administration. H. E. Himwich, D. E. Cameron, E. Homburger and F. Feldman (83), who also used this method, found normal average values in 33 depressive psychotics. They concluded that the cerebral blood flow was normal in these patients and found no significant changes after electro-convulsion therapy. D. E. Cameron, H. E. Himwich, S. R. Rosen and J. Fazekas (84) reported normal cerebral arterio-venous differences in senile patients who showed slowing of the arm-to-carotid circulation. They suggest that a "normal" value under these circumstances indicates a diminution of cerebral oxygen consumption, if slowing of the cerebral circulation can be presumed. C. F. Schmidt (85, 86) found in the course of his experimental work on animals, that changes in the arterio-venous oxygen difference were related to changes in cerebral metabolism, and that the best correlation was that of the volume of circulating cerebral blood with the cerebral metabolic rate; the blood supply is regulated by the metabolic requirements of the brain and this is not directly influenced, within wide limits, by a reduction of the blood supply. After administration of a convulsant the cerebral oxygen consumption is increased and the blood flow is correspondingly raised; conversely, the metabolic rate and the blood flow may both be lowered after the administration of an anaesthetic drug.

It is evident that the presence of several interdependent variables, which are not estimated separately, makes it impossible to draw other than tentative conclusions from estimations of the volume of circulating cerebral blood. If the available methods can be trusted they reveal no important deviation

from normal values in "functional" mental illness, whereas in some "organic" conditions, such as cretinism, mongolism and phenylpyruvic mental deficiency (H. E. Himwich and J. F. Fazekas (87)), and in severe cerebral atrophy (M. Rosenbaum, E. Roseman, C. D. Aring and E. B. Ferris (81)), cerebral metabolism is probably diminished. Negative findings in functional psychoses do not preclude finer circulatory or metabolic derangement, and the absence of major changes is not unexpected in the absence of gross structural or metabolic defect. Moreover, the absence of cerebral circulatory changes at the onset and termination of sleep (other than those depending on the systemic blood pressure), is proof that mental awareness can be reduced without appreciable simultaneous reduction of the cerebral blood flow (F. A. Gibbs, E. L. Gibbs and W. G. Lennox (88)). Accurate and regional estimations of the cerebral circulation in human beings, during altered states of mental activity, are impossible with present experimental techniques.

Report on Clinical Observations and Comment.

In the following paragraphs observations on the vascular system and circulation of patients of this hospital, some of them already detailed in preceding sections (cutaneous responses, state of the blood vessels, blood pressure and result of treatment, etc.), are related to the work of other observers, summarized above.

Post Mortem Examination.

Only one patient suffering from severe peripheral cyanosis, a catatonic female aged 45, died of an intercurrent illness while under observation. The absence of any gross abnormality in her vascular system was confirmed at autopsy. Sections showed slight hypertrophy of the circular muscular coat of the medium and small arteries of the extremities, but thickening of the muscle was practically within normal limits. Findings at autopsy, on 25 other schizophrenics, both male and female, recorded here during the last 10 years, corroborated the observations of N. D. C. Lewis (44) on more extensive post mortem material. The heart of catatonic subjects was always small, their limb vessels were of small calibre and appeared to be thick-walled for their size, but were otherwise normal. The thinness of the auricular wall (atrium) was often remarkable, a point which does not appear to have attracted the attention of other observers. It was frequently of the consistency of tissue paper, only a few strands of muscle fibre being visible under the serous pericardium. In spite of this atrophy, the auricles were not dilated. The ventricular musculature was normal or even slightly hypertrophied. Autopsy on affective, senile and organic psychotics, who had died from an intercurrent illness, did not show the same reduction in the size of the heart, or the same degree of atrophy of the auricular musculature. The vessels of the brain were examined in every case, but owing to variations in size of one or other vessel (commonly seen in both normal and psychotic individuals), no comparative evaluation of the size of these vessels was found possible.

Average Blood Pressure.

The average blood pressure of refractory, mainly catatonic patients was found to be lower than that of paranoid and socialized schizophrenics and of non-schizophrenics, as has already been reported. These observations are in agreement with those of others, R. G. Hoskins and E. M. Jellinek (50) and H. Freeman, R. G. Hoskins and F. H. Sleeper (53), etc.

No reference was found in the literature to a significantly lower blood pressure and pulse pressure in so-called "refractory schizophrenics," compared with socialized schizophrenics, but as the former frequently display catatonic features this difference confirms the recognized tendency to a low systemic blood pressure in catatonic patients.

A rise of systemic blood pressure was found to coincide with mental remission and clearing of peripheral cyanosis. D. E. Cameron and E. M. Jellinek (56) have also noted a rise of blood pressure in patients who had a remission after insulin treatment, and M. J. Farrell and E. Vassaf (57) noted the increased size of the heart after this treatment. It is difficult to explain how relaxation of the peripheral arterioles and the consequent increase in the cutaneous bed can coincide with a rise of systemic blood pressure, unless there is a simultaneous increase in the volume of circulating blood, or a blood-shift. Neither of these possibilities has been satisfactorily investigated.

A rise in blood pressure after the administration of sodium chloride or doca coincided in some of these cases with mental improvement; this suggests that changes in water and salt metabolism may play a part in the physiological adjustment which determines or accompanies the onset of a remission. Patients who were kept under observation after E.C.T. showed clearing of cyanosis within a few hours, but dehydration, if present, was not corrected in these cases by water or salt intake. There are some indications in the literature, to which reference is made later, that increased activity of the suprarenal cortex is one of the relevant factors, responsible for improvement following physical treatment. Increased adrenal activity may account for the improvement shown by patients whose blood pressure had been lowest before insulin therapy, as reported by D. E. Cameron and E. M. Jellinek (56); a cortical deficiency may have been corrected by this treatment. D. I. Abramson (17) observed an improvement in the circulation of the hands of schizophrenic patients after insulin treatment.

Retinal Circulation.

The retinal vessels of 150 female and 50 male psychotics were examined here; approximately two-thirds of these patients were suffering from a schizophrenic illness, the others from various affective psychoses. Fifty medical students were used as controls. Many of the schizophrenic patients, both male and female, were found to have tenuous retinal arterial trees, compared with affective patients and normal controls. The difference was particularly noticeable in restless young schizophrenics who suffered from severe peripheral cyanosis and other vascular abnormalities, such as contraction of the main limb vessels. Their retinal arteries were often thread-

like, irregular in calibre and in part empty. The retinal veins were usually normal in appearance, therefore considerably larger than the corresponding arteries, and the venous blood was frequently very dark. Occasionally the veins were also narrowed and in rare cases, especially in patients who complained of headache after an electrical convulsion, they were dilated and engorged. After a mental remission the changes in the appearance of the retinal vessels were sometimes striking; filiform vessels were absent, the arteries were wider and showed better filling. It was not found possible to estimate the percentage of patients who had definite narrowing of their retinal arteries, as day to day variations in calibre were almost the rule; while some branches remained strikingly tenuous, others had a normal appearance. Under observation, contraction and emptying of a section of a retinal artery, with a movement resembling peristalsis, was not infrequent in schizophrenic subjects, but was never observed in affective psychotics or in normal controls.

These retinal changes are very similar to those described by J. M. Cotton, N. D. C. Lewis and A. W. Egenhofer (61), but in the cases observed here, increased vascularity was only seen after remission and could not be used as the prognostic sign suggested by these authors. Nolan Lewis and his associates succeeded in measuring the calibre of the retinal vessels. A similar objective measurement was attempted with a Decagon (C. D. Keeler) ophthalmoscope, but patients were unwilling to submit to the prolonged examination necessitated by this difficult technique, which is probably only reliable in expert hands.

The Relation of Peripheral Vasoconstriction to the Mental Syndrome.

E. Guttmann's suggestion (69) of related peripheral and cerebral vascular disturbances in confusional states of Raynaud's syndrome, is supported by the post-operative study of a female patient aged 35, who suffered from severe Raynaud's disease and presented interesting mental changes following a right cervical sympathectomy (division of the second and third thoracic rami and of the chain below this level). Blanching of the right side of the face was noted when the patient returned to the ward after her operation, and lasted approximately half an hour. Four hours later the temperature of the right side of the face had risen 1° C. higher than that of the left, due possibly to reactive hyperaemia, as the right side of the face was now flushed. Examination of the fundus of the eyes at this time showed the right retinal arteries to be contracted in comparison with those of the left side. On the following day the patient was slightly confused, difficult to interest and gave childish answers, repeating frequently: "I am making a fool of myself." She could see objects with either eye and could find them with her right hand, but only when they were placed to the right of the mid-line; she could not find them with her left hand, which groped in the right field, wherever they were placed. She was repeatedly asked to count fingers, but she could not, or would not do so, became agitated and repeated that she could see them. She recognized objects placed in her right palm, but not when they were placed in the left palm and mistook a farthing for a cake of soap "because it was sticky." Left hand movements were clumsy, right hand movements were normal. No

neurological changes were elicited, neither weakness nor abnormal reflexes, and the pupils were equal and active. Testing for sensation was inconclusive, as she was distractable and her answers were unreliable. No hemianopia developed and 48 hours after the operation her mental condition was dull but otherwise normal; interest in the left visual field had returned; she was again able to find objects situated in either field with either hand and now recognized them when they were placed in either palm. There was no longer any difference in the calibre of the right and left retinal arteries when the fundus was re-examined about 20 hours after the operation.

This case, which showed transient overstimulation of the cervical sympathetic of one side, followed by some transient mental symptoms and neurological dysfunction, seems worth recording as it throws light on similar symptoms occurring after less extreme sympathetic overactivity in cases of severe Raynaud's disease and migraine. It is possible that the coincidence in psychotic patients of retinal vasodilatation and mental remission is of some significance, an indication of improved cerebral blood supply coinciding with improved mental functioning. In patients who suffered from cyanosed extremities, no exacerbation of mental symptoms was observed during periods of increased peripheral vasoconstriction (with the possible exception of increased restlessness), but the coincidence of a mental remission and clearing of peripheral cyanosis was so common that it could hardly be a fortuitous circumstance. It suggested the presence of a common factor underlying both these occurrences.

Inhalation of Mixtures of Carbon Dioxide.

Inhalation of a mixture of 30 per cent. carbon dioxide in oxygen from a mask loosely held to the face, was used in an attempt to dilate contracted retinal vessels. This it invariably succeeded in doing and it produced some other changes which are also recorded here.

Eighteen schizophrenic female patients with contracted retinal arteries showed widening of these vessels and arterialization of the veins 3 to 5 minutes after the onset of inhalation, which persisted for some minutes after interruption of inhalation 8 minutes later. Twelve of these 18 subjects showed a temporary mental improvement which lasted up to a few hours. Catatonic patients who had previously been mute answered questions, became accessible and sometimes gave the superficial impression of being mentally almost normal, while others showed no mental changes or became excited and noisy. None of these patients was permanently benefited by 18 to 24 daily sessions of carbon dioxide inhalations. Three depressed patients were also treated; their retinal vessels were normal at the onset and showed no change later, neither was there any mental improvement after a course of 6-12 daily inhalations.

An incidental and unexpected occurrence in 10 of 18 female schizophrenics who had suffered from prolonged amenorrhoea, was re-establishment of the menstrual cycle after 3 or more daily sessions of carbon dioxide inhalations.

These observations are in line with those of S. Cobb and F. Fremont-Smith (70) who noted arterialization of the retinal veins, and those of A. S.

Loevenhart, W. F. Lorenz and R. M. Waters (72) and others, who reported temporary mental brightening and increased accessibility of catatonic patients after inhalation of carbon dioxide. Re-establishing of menstrual function, to which reference is again made later, does not appear to have been previously observed. It bore no obvious relation to the patients' state of mental alertness, as some patients were mentally brighter after a course of carbon dioxide inhalations, while others remained unchanged.

Salt and Doca Administration.

These substances were used to raise the blood pressure of asthenic female schizophrenics who had suffered from marked hypotension and they seemed to favour the onset of a mental remission in a few cases.

In normal persons mental effort is accompanied by a rise of blood pressure following peripheral vasoconstriction. During a mental remission a psychotic may show a rise of blood pressure which coincides with improved mental function and is accompanied by peripheral vasodilatation. It is not known whether this rise of blood pressure can be explained by an increase in blood volume or by a blood shift. It has been suggested that increased adrenocortical activity may account for improvement of the circulation under these circumstances, although there is no evidence to show how the blood pressure is raised.

Many of the studies which deal with the somatic aspects of catatonia refer to the circulatory deficit, contracted vessels, small heart, low blood pressure and peripheral cyanosis of these patients. One may perhaps conclude that a "functional psychotic" who suffers from circulatory defect is more likely to show a catatonic than a paranoid or affective syndrome. If one went further and attributed aetiological significance to the vascular deficiency it would be difficult to explain why all catatonics do not suffer from this defect, and why it is occasionally present in other psychotics and in persons who do not suffer from mental illness. It is more likely that a vascular deficiency may facilitate the mental and physical changes underlying the characteristic withdrawal of catatonic patients and that this withdrawal is hindered by a more efficient circulation. If this is the case it should be possible to alleviate the psychotic syndrome by remedying the vascular defect. Final proof is lacking, but the apparent benefit derived from physical methods of treatment which are known to raise the blood pressure, such as cortical extracts, salt, carbon dioxide, possibly insulin and E.C.T., is not inconsistent with this view. A remission is such a complex psychosomatic event that it probably never results from a change limited to one level of the personality, although clinical evidence suggests that therapeutic changes may be initiated at either the physical or mental level. As in other biological reactions which involve the whole personality, part-events must concur and the total response will be much the same wherever the reaction is started; total responses are identical whenever therapeutic success is complete. Precedence in the order of part-responses, or differences in their quality, might serve to indicate the relative importance of one or other remedial measure, but unfortunately these part-

responses are seldom consecutive, they are more usually cumulative, as if mutually facilitated at various levels of the personality.

METABOLISM, NUTRITION, HEAT REGULATION AND BODY TEMPERATURE OF SCHIZOPHRENIC PATIENTS.

Basal Metabolic Rate.

The methods at present available for the estimation of the basal metabolic rate are difficult and unreliable when applied to psychotics, as they presuppose a degree of co-operation which is not easily secured; experimental conditions require special departments, trained personnel, costly apparatus and preferably the use of air-conditioned rooms. None of these requisites are usually available and work which has been carried out under "basal conditions" comes almost exclusively from the research departments of the United States. It is gratifying to note that information gained by earlier investigators who have worked under much less favourable conditions has, on the whole, been confirmed by these more elaborate clinical experiments.

An early study of the basal metabolic rate of a mental patient was published by T. Raphael, J. P. Parsons and M. N. Woodwell (89) who found that the metabolic level of a young male catatonic was 21-29 per cent. below the average normal value, in spite of a high calorie diet administered by tube feed. After clinical improvement the metabolic rate of this patient rose to 105 per cent. K. M. Bowman and G. P. Grabfield (90) have noted that in only 4 of their 50 organic and functional psychotics the metabolic rate was 10 per cent. above the average normal value. Very low levels were the rule in schizophrenic patients; in some of these cases the metabolic rate was as low as minus 37 per cent., although malnutrition or simple hypothyroidism could not be blamed for this depression of the metabolic level. C. B. Farr (91) confirmed the low metabolic level and great variability of the basal metabolic rate of patients suffering from dementia praecox, while in psychotics suffering from mood disorders more normal readings were obtained.

The metabolic studies of R. G. Hoskins and his collaborators have extended over more than 10 years. After reviewing all the cases reported in the literature and his own observations on 214 male schizophrenics (92) Hoskins concludes that the average oxygen consumption of these patients is about 88 per cent. of normal value, with extreme readings of 57 per cent. and 122 per cent. Hoskins' patients were typed by 4 psychiatrists; a low and almost equal rate of oxygen consumption was found in patients belonging to the catatonic, hebephrenic and paranoid sub-groups, slightly higher values in those described as "simple" schizophrenics. Hoskins believes that the basal oxygen consumption of the whole group is in reality lower than the calculated 88 per cent., as many patients remained tense during these estimations; he suggests a corrected reading nearer 75 per cent. of the normal consumption. J. C. Rheingold (54) also found some very low metabolic levels in 129 early (male and female) cases of schizophrenic illness investigated by him; the B.M.R. was often as low as minus 40 per cent., and in only two cases was it above 110 per cent.; a rise in the metabolic level was found to

coincide with clinical improvement. Rheingold estimated the metabolic rate in 30 schizophrenic patients before and after exercise and recorded the interesting observation that in 11 of these patients the metabolic level was depressed further by physical exertion.

Qualitative Metabolic Changes.

Very little is known about the factors which cause depression of the general metabolic level in schizophrenia; the evidence in favour of endocrine dysfunction is discussed later, but it is interesting to note here that qualitative metabolic changes have been reported by various observers. The decreased specific dynamic action of proteins has been described by S. Fischer (93, 94) who observed that the rate of oxygen consumption of these patients was not merely depressed, but that it failed to rise after protein ingestion. This metabolic failure was primary and it was followed later by a fall in the basal metabolic rate; both levels remained low while the mental illness persisted and rose again after recovery from the psychosis.

Other investigators have attributed the metabolic failure of schizophrenic patients to a change in hydrogen ion concentration. H. Greving (95) found evidence of overcompensated acidosis and threatened alkalaemia in 102 of 157 schizophrenics investigated. D. Jahn (96), who had previously described this metabolic error, spoke of an "asthenic metabolic change" which is aggravated by muscular work and is only observed in patients of leptosome type, never in pyknic subjects. Both Greving and Jahn have related this metabolic abnormality to dysfunction of the liver and depletion of glycogen, a change which is similar to that seen in starvation and in secondary ketonuria. H. H. de Jong (97) found evidence of liver dysfunction and a positive cephalin-cholesterol flocculation test in catatonic patients. O. Lingjaerde (98) and other observers have reported similar disturbances of liver function which were evidenced by ketonuria, increased urobilin excretion and various positive turbidity tests, while G. Lundquist (99) noted another abnormality, the loss of regular rhythmic diurnal variations of serum protein.

Post mortem evidence of liver atrophy, shown by shrunken parenchyma and paucity of glycogen, was observed by Lingjaerde in 8 of 10 cases he examined; the histological appearance differed from that of cirrhosis due to back pressure and venous stasis and was consistent with a degenerative lesion of the parenchyma. Somewhat similar appearances of the liver parenchyma are described by P. J. Reiter (100). He attributed the changes found at autopsy to the late results of intestinal toxæmia.

The difficulty of excluding changes which are due to a terminal illness make these post mortem findings inconclusive, but taken in conjunction with numerous reports on liver dysfunction, recorded by many observers, there is an impressive array of evidence in favour of liver damage in schizophrenia. Altered vascularity of the liver and deficient oxygenation of the liver cells are suggested by the observations of C. S. Davidson, J. H. Lewis and H. J. Tagnon (101), who found similar degenerative lesions, and occasional necrosis of the centre of the liver lobule, in medical patients who had suffered from

peripheral vascular deficiency and a low blood pressure during a severe acute illness. Quite recently B. Maegraith, W. H. H. Andrews and D. Gall (102) have given support to this interpretation of the liver disturbance by publishing some observations on a "hepatic syndrome of wide distribution" which offers the histological picture of central zonal degeneration and sometimes progresses to necrosis. This is, according to these observers, a non-specific reaction due to stagnant anoxia, probably following reflex constriction of some part of the hepatic venous tree; the relevant reflexes are said to arise either within or outside the liver. It is tempting to suppose that disturbances of liver function and liver structure in catatonic schizophrenics may be of this nature, as excessive constriction of the limb vessels and retinal arteries, and a low blood pressure are common features in these patients. It would be of great interest to study the structure of the schizophrenic liver during life by means of liver puncture.

Frequent reference is made in the literature to the similarity of anoxic and schizophrenic symptoms; changes in behaviour, insidious deterioration, wasting, excretion of a larger volume of urine have all been described in anoxic patients (H. G. Armstrong (103)). R. G. Hoskins (104) has drawn attention to the resemblance of these symptoms to those occurring in schizophrenia, a similarity which had already been noted by R. A. McFarland (105). He added some further symptoms common to both conditions, diminution of attention, perseveration, inappropriate affect, impaired judgment, etc. In an earlier article R. G. Hoskins (106) had described the elimination of an increased volume of urine by schizophrenic patients and in a later publication G. A. Brown and his associates (107) drew attention to the occurrence of mental confusion, hallucinosis and occasional hyperkinesia in anoxia.

Malnutrition.

Malnutrition in chronic schizophrenics has been studied by many observers, including C. N. Baganz and J. M. Norris (108). These authors investigated its incidence in a group of 374 schizophrenic patients, of an average age of 38 years, and found that it was no greater on their admission to hospital than that occurring in the other 1,164 psychotic in-patients of the institution; it was present in 52 per cent. of the former and 56 per cent. of the latter. Eight years later the incidence in the general hospital population had fallen slightly, to 50 per cent., but it had risen to 62 per cent. in the original group of schizophrenics; 44 per cent. of the latter and only 30 per cent. of the general hospital population were now more than 10 lb. underweight. H. C. Sharp and C. N. Baganz (109) had previously noted that the loss in weight was as great in schizophrenic patients who were fed on a diet of 4,500 calories, administered by tube feed, as in other schizophrenics who received the ordinary hospital diet. The degree of malnutrition was found by Baganz and Norris to be inversely proportional to the amount of activity displayed by these patients, being greatest in those who were completely idle.

The remarkable improvement in physical condition which follows a course of small daily doses of insulin is too well known to require stressing; it has

been described, among others, by H. C. Sharp and C. N. Baganz (109). No satisfactory theory has yet been advanced to explain the therapeutic action of insulin in schizophrenia. The malnutrition of these patients is not relieved, as a rule, by the ingestion of a rich diet of high caloric value, but is remedied by the administration of insulin.

Heat Production and Body Temperature.

An interesting study by W. Mayer-Gross and F. Berliner (110) illustrates several features of the mechanism of heat production and heat regulation. These authors have found that the fall of rectal temperature, which can be observed during insulin hypoglycaemia, is of central origin and is probably due to carbohydrate depletion. It occurred while adrenaemia was still present and when it preceded the onset of coma it sometimes coincided with a period of increasing hyperkinesia. In the absence of coma there was as a rule no fall of body temperature; a rise of temperature occurred simultaneously with the termination of coma. As the tone of the muscles is raised during hypoglycaemic coma it is impossible to attribute a fall of body temperature in this condition to muscular atonia. The observation is a useful reminder that an unexplained fall of body temperature and metabolic level should not be ascribed to the loss of muscle tone when no other explanation is at hand; our information about the physiological processes which govern heat production is still incomplete.

We possess evidence for the existence of a hypothalamic heat-regulating centre, which was demonstrated by animal experiment and was localized in man by pathological lesions and surgical interference. We also have evidence of the interplay at the hypothalamic level of two mechanisms, of heat production and heat regulation, which are probably spatially distinct, but we know little about the peripheral mechanisms by which heat production is raised, or the hormonal and nervous agents which govern these reactions. S. W. Ranson and H. W. Magoun (111) consider that shivering and increased muscle tension are the usual means by which body heat is generated during exposure to cold. Their theory leaves the fall of body temperature which occurs during hyperkinesia unexplained and it does not help to explain the low body temperature of catatonic patients whose muscle tone is frequently raised, who have not lost their ability to shiver and are often restless and overactive. If, on the other hand, muscle work (as distinct from muscle tone) is necessary for preserving an even body temperature, a fall in the metabolic level after physical exercise, observed in some schizophrenic patients by J. C. Rheingold (54) and H. Greving (95), is beyond comprehension. It is also impossible to explain on this supposition the observation recorded by S. M. Horvath, H. Golden and J. Wager (112), that 45 young men, clad in arctic uniform, who sat quietly for 3 hours in an atmosphere of minus 40° C. maintained their internal temperature with slight loss and without an appreciable increase in muscle tone, in some cases without noticeable shivering, although their basal metabolic rate was almost doubled. As early as 1922 the importance of muscle tone for the maintenance of an even body temperature had been questioned by E. Grafe (113) who had noted that oxygen consumption

was not raised by increased muscle tone in catatonia, or in decerebrate and Parkinsonian rigidity.

With these gaps in our knowledge it is obviously impossible to explain the failure of heat production which is reflected in the low basal metabolic rate and low surface temperature of catatonic patients. We still lack information on the metabolic requirements of persons experiencing excitement, depression or mental withdrawal. The qualitative metabolic disturbances which are observed in schizophrenic patients may, like their vascular deficiencies, favour the onset of the psychosis without being essential to its occurrence.

Skin Temperature.

Numerous studies on the temperature of the extremities of psychotic patients are reported in the literature. D. E. Cameron (18) has recorded 10,000 temperature readings in 50 schizophrenics and an equal number of non-schizophrenic controls. He concluded from his observations that heat production is diminished and the control of heat loss is active in these patients; their body temperature was found to be lower throughout the day than that of non-schizophrenic controls. H. Freeman (114) compared the temperature of schizophrenic patients to their paired normal controls and found that at room temperature 15° C. (59° F.) the skin temperature of the trunk and of the proximal part of the limbs of these patients was slightly higher than that of the normal controls. Their rectal temperature was not significantly lower, although cooling of the body was more rapid than that of the controls. These differences are ascribed by Freeman to dysfunction of the neural mechanisms controlling vasoconstriction. A simple explanation, vasoconstriction compensating for low heat production, is disregarded by this observer.

B. Mittelman and H. G. Wolff (115) have studied the effect of various emotional states on finger temperatures. When fear, pain or stress were experienced, the finger temperature was lowered, irrespective of environmental conditions, but in persons who suffered from Raynaud's syndrome the vasoconstrictor response initiated by emotion or by increased mental activity was superimposed on vasoconstriction due to chilling. The fall in temperature which accompanied mental activity and emotional tension was greatest when the vessels were initially dilated, during mental relaxation and during sleep. Changes in the peripheral surface temperature, which were noted by these authors, are a reminder that pre-existing physiological conditions and affective mental states should be taken into consideration before claiming excessive cooling or abnormal cutaneous reactions for any class of patients under given conditions of observation.

The Relation of the Surface Temperature to the Metabolic Rate of Man.

In two investigations of practical interest the metabolic rates of normal experimental subjects were related to their respective foot temperatures. C. Sheard and M. M. D. Williams (116) found a simple linear relation between the metabolic rate expressed in calories per unit body surface and the temperature of the big toe. This relation was, however, of a "dual character," as

subjects tended to cluster round two levels, a higher and a lower level of foot temperature; this subdivision, which was not based on sex, was related to body build and separated the stout from the lean and those who had a dry skin from others who had "cold, clammy extremities." It became evident to these observers, after a great number of measurements had been recorded, that thermostasis was mainly dependent, in normal subjects, on regulation of the peripheral blood flow, particularly that to the lower extremities. Under basal conditions an average toe temperature of 24.8°C. and a finger temperature of 34.1°C. were found to correspond to a metabolic rate of minus 14 per cent., whereas a toe temperature of 31°C. and a finger temperature of 34.6°C. correspond to a metabolic rate of minus 0 per cent., the toe temperature proving a better indicator of the metabolic rate than the finger temperature. The metabolic rate of these subjects, at room temperature 77°F. (25°C.), showed individual variations between 38 and 44 calories per square metre body surface per hour. A rise or fall in the toe temperature of approximately 1°C. was found to be equivalent to an increase or decrease of one-half to one calorie per square metre body surface. Very similar observations had previously been recorded by W. G. Maddock and F. A. Collier (117) who had worked with a smaller number of cases and had used indirect calorimetric measurement: under constant environmental conditions the temperature of the extremities, particularly that of the toes, was found to reflect the level of heat production. O. L. Kirklin, W. A. Plummer and C. Sheard (118) drew attention to a fall in the temperature of the toes after thyroidectomy or Lugol medication, which corresponded to the reduced metabolic level, while finger temperatures did not follow the same downward curve. A rise in the toe temperature, on the contrary, was observed in patients who suffered from exophthalmic goitre.

Differences in the Metabolic Rate of the Two Sexes.

In a study of the basal metabolic rate of 129 patients suffering from early schizophrenic illness, J. C. Rheingold (54) found a comparatively lower metabolic level in female psychotics. E. F. Du Bois (119) concluded from his own work, and that of others, that, in general, men have a uniform basal metabolism over a wide range of environmental temperature, whereas women show a reduction of metabolism in the warm zone, minimal values between 29°C. and 33°C. , and higher rates when exposed to lower or higher temperatures.

Report on Clinical Observations and Comment.

The majority of patients observed here were not suitable subjects for basal metabolic examinations, but four stuporous female catatonics who gave reliable readings showed a metabolic rate between 65 per cent. and 75 per cent. of normal value. A low metabolic level was inferred in other schizophrenics from a low surface temperature, particularly that of the toes. These surface temperatures were relatively lower in female schizophrenics and mental defectives than in comparable groups of male patients, as has already been reported. If the linear relation of metabolic rate to toe temperature, which

was observed by C. Sheard and M. M. Williams (116) and by W. G. Maddock and F. A. Collier (117) in normal persons holds good for psychotics, the very low surface temperatures recorded in these patients are evidence of a greatly reduced metabolic level. Their toe temperatures conformed to environmental conditions, as was previously observed by O. L. Kirklin, W. A. Plummer and C. Sheard (118), but their finger temperatures varied from hour to hour, independently of environmental conditions and subject to affective control, confirming the observations of B. Mittelman and H. G. Wolff (115) on non-psychotic subjects. No evidence was available to confirm or contradict Du Bois' observation that a lower metabolic level obtains in female subjects at room temperatures between 29° C. and 33° C., the indoor temperatures at which these patients were observed being always lower than 29° C. Schizophrenics and affective patients had almost identical surface temperatures when they were examined together in a warm room, but in cooler surroundings the surface temperature of the schizophrenics usually sank much lower than that of affective patients. As air-conditioned rooms were not available and as the patients were not stripped of all their clothing, no claims are made to exact temperature measurement; examination under the same environmental conditions failed however to show any constant difference between the rate of cooling of schizophrenic and affective patients. The loss of heat, expressed in degrees centigrade, was sometimes greater in the latter, when their initial temperature had been higher. Schizophrenics only differed from non-schizophrenics by their relatively low skin temperature, both before and after exposure of their bared limbs to moderate room temperatures. In a few cases there was no rise or fall in the toe temperature of schizophrenic patients after strenuous exercise. J. C. Rheingold (54) has also recorded a fall in the metabolic rate of some of his patients after physical exertion.

Reflex vasoconstrictor responses of schizophrenic patients were no brisker than those of normal subjects and were readily elicited, whereas vasodilator responses were more common in affective psychotics after reflex cutaneous stimulation.

The available evidence suggests that excessive peripheral vasoconstriction in schizophrenic subjects, which is particularly evident in catatonic patients, is part of the normal physiological mechanism for conserving body heat. Prolonged vasoconstriction is necessary in the case of these psychotics owing to their failure to respond to increased bodily requirements during chilling and muscular exercise, by adequate rises in metabolic level.

DYSFUNCTION OF THYROID, PITUITARY AND ADRENAL GLANDS IN SCHIZOPHRENIC PATIENTS.

Thyroid Dysfunction and Replacement Therapy.

The somatic manifestations of schizophrenia are sometimes ascribed to thyroid deficiency. A loss of cutaneous elasticity, low blood pressure, low metabolic rate and slowing of mental processes are common in schizophrenics, whereas signs of increased thyroid activity have seldom been recorded. R. E.

Hemphill (120) who describes five cases of hyperthyrotic schizophrenic illness is at pains to stress their rarity.

The effect of thyroid medication in the treatment of schizophrenia is the subject of many publications. C. B. Farr (91) found that prolonged courses of thyroid therapy were followed by little improvement and that thyrotoxic symptoms were rare, even after heavy dosage. A poor response to thyroid treatment was also observed by K. M. Bowman and G. P. Grabfield (90) who concluded that the low metabolic rate of these patients could not be the result of simple hypothyroidism. R. G. Hoskins and F. H. Sleeper (121) expressed the opinion that some schizophrenics were benefited by large daily doses of up to 60 gr. of desiccated thyroid, given over several weeks. A failure of oxidative cell enzymes is suggested by R. G. Hoskins (122) as a possible cause of unresponsiveness to thyroid treatment in schizophrenic patients.

A favourable therapeutic action of thyroid hormone is claimed by R. Gjessing (123) in periodic catatonia. After depletion of the nitrogen stores of the body by thyroid treatment there was no recurrence of the active, stuporous or excited phases of the illness, or further alternating swings of positive and negative nitrogen balance. S. W. Hardwick and A. B. Stokes (124) were able to confirm some of Gjessing's findings, but they observed that the swings in nitrogen balance of these patients were related to their state of general nutrition and could be avoided by improved nutrition, without interfering with the rhythm of the mental illness.

Eight male schizophrenics were treated by L. H. Cohen and J. H. Fierman (125) with large doses of up to 36 gr. of desiccated thyroid daily. These patients failed to show more than a temporary rise of their metabolic level and no thyrotoxic symptoms, in spite of this heavy dosage. J. C. Rheingold (54) who treated 129 male and female schizophrenics with thyroxin, also failed to raise their metabolic level and concluded that schizophrenic patients were either unable to elaborate thyroxin in their tissues or that the hormone was inactivated by an antibody. Rheingold accepts the evidence in favour of a central thermoregulatory action of thyroxin, the inhibitory effects of barbitone being best explained by the antagonistic action of these substances on the metabolic centre situated in the hypothalamus.

A central action of thyroxin is also postulated by B. Issekutz and B. Issekutz Jr. (126) who noted the absence of metabolic responses to this hormone when it was given to poikilothermic animals, or to cats, following luminal administration or decapitation. B. Kommerell (127) attributes a disproportionate rise in oxygen consumption, when muscular work is performed after thyroxin medication, to the action of the hormone on the central nervous mechanism; this increase in oxygen consumption is considered by Kommerell to be a counterpart of the "sparing reaction" obtained by training and improved muscular co-ordination. M. L. Turner (128) quotes similar evidence in favour of a central action of thyroxin, which is evidenced by increased bodily activity in animals treated with thyroid extracts. It is usual in clinical practice to consider that improvement in the mental functions of treated myxoedematous patients has resulted from the action of the hormone on the cells of the central nervous system, either assisting their metabolism or removing oedema. Some

support is given to this theory by an increase in alpha-wave frequencies observed by M. A. Rubin, L. H. Cohen and H. Hoagland (129) in 4 schizophrenic patients after thyroxin medication. H. E. Meyer (130) supports the theory of a central action of the hormone on clinical grounds; he considers that post-encephalitic "Basedow syndromes" are due to morphological changes in the hypothalamic centres on which the hormone exerts its action. Possibly a diminished response to thyroxin is the result of functional hypothalamic changes in schizophrenic patients, but experimental support for this theory is still lacking.

It is surprising that there is so far no agreement on the peripheral action of thyroid hormone and that contradictory statements are found in the literature concerning the effect of thyroxin on the oxygen consumption of isolated tissues. D. Rapport, A. Canzanelli and R. Guild (131) are of the opinion that thyroid medication increases the metabolic rate of tissues which are subsequently isolated. If an animal is subjected to thyroidectomy before this assay, the rise in the metabolic rate of its tissues is sufficiently great to be easily recognized and the reaction can be used as a "spot test" for thyroid preparations and their inhibitors.

A clinical study on the relation of thyroid therapy to serum iodine and metabolic rate, published by D. S. Riggs, E. B. Man and A. W. Winkler (132), confirms the dependence of the basal metabolic rate on the precipitable fraction of serum iodine (a correlation given as 0.82 ± 0.05 in Moulton's *Chemistry and Physiology of Hormones*, Washington, 1944). These authors found that in 4 schizophrenic patients investigated by them, a poor response to thyroid medication was offset by a good correlation of organic serum iodine and metabolic rate. The response of these patients to thyroxin therefore resembled the normal response rather than that of myxoedematous subjects. While these schizophrenics only responded to thyroxin given in massive dosage (10 grs. or more of desiccated gland daily), much smaller doses were effective in myxoedematous patients used as controls. The correlation of the metabolic rate and the organically bound serum iodine remained good in all the cases investigated, in 4 schizophrenics, 6 other euthyroid subjects, and in 7 myxoedematous patients. Inactivation of the hormone was considered to be possibly more rapid in euthyroid cases, but the metabolic response to a rise in organically bound serum iodine was at least as good as that of myxoedematous subjects; there is therefore no evidence of diminished tissue sensitivity in these patients.

The association of a mental disturbance with myxoedema and of a metabolic deficiency with schizophrenia has tended to confuse these two conditions, but H. Zondek and G. Wolfsohn (133) believe them to be entirely separate and point to the success of replacement therapy in myxoedema. There is almost unanimous agreement on the limited usefulness of thyroid treatment in schizophrenia. Few successful cases have been reported and these may have suffered from true hypofunction of the thyroid, similar to myxoedema. R. Gjessing's claim that relief of mental symptoms follows thyroid medication is limited to the rare cases of periodic catatonia and still awaits confirmation.

While the cause of a low metabolic level in schizophrenia remains obscure, the clinical failure of thyroid therapy seems to have been established; a primary reduction of thyroid function can probably be excluded by failure of

replacement therapy. Excessive destruction of the hormone, or a possible change in the nervous centres on which the hormone acts, might explain this failure, but both theories lack experimental support.

Pituitary Dysfunction.

Defective action of the pituitary gland and secondary thyroid dysfunction have been suggested by several observers as possible causes of metabolic failure in schizophrenic patients. In non-psychotic subjects who suffer from anorexia nervosa and share some of the common somatic manifestations of catatonia, a low metabolic rate and peripheral vascular disturbances, R. Greene (49) has reported relief of these symptoms after replacement therapy with thyrotropic hormone (Thyrogan). S. Fischer (134), who showed that the metabolic response to ingested proteins was diminished in schizophrenic patients, believes this to be evidence of impaired function of the anterior lobe of the pituitary gland. After treating his cases with a "pituitary-like substance," isolated from the urine of pregnant women, he observed satisfactory therapeutic results. It is interesting to recall that the cure of Raynaud's syndrome was observed by T. Lewis (6) to coincide with the onset of Grave's disease, in which the output of thyrotrophic hormone is probably raised. As the thyrotrophic fraction of pituitary hormone has now been successfully isolated, it should be possible to test substitution therapy on a wider scale in schizophrenic patients.

A failure of pituitary adrenocorticotrophic hormone secretion is suggested by abnormal physiological reactions of schizophrenic patients to psychological stresses, to which reference is made later, and the failure of gonadotrophic hormones is suggested by disorders of sexual function, discussed in the section dealing with those disorders.

Metabolic Responses to Cold.

It has long been known that a rise in the metabolic level is the physiological response to chilling, but the mechanism by which this rise is made possible is imperfectly understood. Recent experimental evidence has shown the importance of the thyroid gland in this reaction. In animals exposed to cold there is a great increase in both the vascularity and the size of this gland and an increase in the height of its follicular epithelium (I. Ariel, F. W. Bishop, and S. L. Warren (41)). Very similar cellular reactions were observed by R. S. Turner and M. L. Turner (135) in chilled slices of thyroid tissue *in vitro*, and were attributed by them to the direct effect of cold, rather than to activation of traces of thyrotrophic hormone in the isolated tissues. In the intact animal similar changes are believed to follow increased pituitary activity and a raised output of thyrotrophic hormone, when the environmental temperature is lowered. The following facts are known: the normal pituitary gland responds to a fall in the metabolic level, or to interference with the thyroid principle (as for instance by thiourea), by an increased output of thyrotrophic hormone (A. S. Gordon, E. D. Goldsmith and H. A. Charipper (136)); chilled peripheral blood has a stimulating action on the thermoregulatory diencephalic centre;

it is suggested that a link may exist whereby the activity of the anterior lobe is stimulated, either directly or via the hypothalamus, by changes in the temperature of the blood reaching these centres from the periphery. It is interesting to note that the direction of the blood flow is from the infundibulum to the anterior lobe of the pituitary, and that the anterior lobe also receives a direct arterial supply from the basal arteries (G. B. Wislocki and L. S. King (137)), whereas few, if any, nervous elements connect the posterior and anterior pituitary lobes. J. D. Green and G. W. Harris (138) have demonstrated by serial sections that the large portal vessels which leave the sinusoids of the median eminence of the human hypophysis enter the pars distalis, and that in the eminence and infundibulum the neural tissue and the sinusoidal loops are in intimate contact. No convincing nerve supply could be traced to the cells of the pars distalis, a humoral transmission of stimuli to the anterior lobe being suggested by these anatomical arrangements.

The anatomical position of the thyroid gland, placed between skin and trachea and therefore exposed to both external and internal environmental temperatures, may facilitate the direct response of the follicular epithelium to cold. The total thermoregulatory reaction is also aided, according to G. C. Ring (139), by the potentiating action of thyroxine on adrenalin. The metabolic and cellular responses to cold are enhanced in experimental animals by a cervical sympathectomy, which eliminates the vasoconstrictor supply of the thyroid gland and increases the blood flow to the thyroid and possibly also to the pituitary gland (G. H. Lowe, A. C. Ivy and S. Brock (140)). Section of the pituitary stalk, on the contrary, was noted by U. U. Uotila (141) to lower the thermoregulatory response by severing the anterior pituitary lobe from the hypothalamic centres which control it; this experiment does not show whether a nervous or vascular link has been divided.

Our information regarding the causes of metabolic failure schizophrenia is still too fragmentary to incriminate any one part of the complex mechanism of heat production and heat regulation, but several new lines of investigation are proposed by these experimental findings.

Adrenal Dysfunction.

Adrenocortical disturbances are suggested by the frequent occurrence of hirsuties in female schizophrenics and by asthenic states, in catatonic patients, which resemble the clinical manifestations of Addison's disease. Polyuria was considered by R. G. Hoskins and E. M. Jellinek (50) to be a characteristic feature of schizophrenic illness, suggesting a disturbance of water and salt metabolism due to hypothalamic or adrenocortical dysfunction.

Four cases of hypertrichosis and raised 17-ketosteroid excretion in female schizophrenics were reported by C. Allen and L. R. Broster (142); the mental illness which antedated the cutaneous disturbance was relieved after unilateral adrenalectomy, although the cutaneous condition did not always improve after this operation. It seems possible that when mental improvement followed the operation, this was not determined solely by removal of one adrenal gland. Increased cortical activity could have resulted from raised adrenotrophic

stimulation, but the cure of the mental symptoms after adrenalectomy cannot be explained by this assumption.

The common physical signs of catatonic patients, their low blood pressure and asthenia, suggest adrenal failure rather than overstimulation, although secondary suppression of the pituitary may follow a rise of adrenocortical activity. It is possible that component fractions of cortical secretion are separately raised or lowered, and that the resulting physiological changes are sometimes masked by the compensatory activity of other endocrine organs, or revealed by differences in tissue responsiveness. We have at present no evidence to suggest which, if any, of these factors is operative in the case of schizophrenic patients who suffer from symptoms of adrenocortical dysfunction.

The complexity of polyglandular reactions is illustrated by the experimental work of M. Vogt (143). He noted that increased output of adrenocortical hormone followed repeated intravenous administration of adrenalin and was accompanied by accumulation of fatty material in the cortex of the adrenal, but actual growth of the adrenal cortex occurred only in animals with a functioning pituitary gland (144). L. P. Herrington and J. H. Nelbach (145) found an increase in the size of the adrenal cortex after animals had been exposed to cold or had been continually disturbed, a possible indirect result of increased secretion of adrenalin; secondary shrinking of the pituitary gland followed excessive growth of the adrenal cortex. The similarity of these adaptations to the "general adaptation syndrome" of H. Selye (146) was noted by these observers.

A different aspect of adrenocortical deficiency has been considered by O. Peczenik (147), who described the fall of body temperature which follows the administration of procaine to experimental animals. Peczenik showed that this fall is greatly increased by adrenalectomy, but that it can be prevented in the intact animal by thyroxin, or by desoxycorticosterone acetate and allied steroids. The protection which is afforded by thyroxin is ascribed to its action on the adrenal cortex, increasing its secretion and leading to its hypertrophy. G. S. Dawes (148) showed that procaine, quinine and quinidine (to which J. H. Burn and N. K. Dutta (149) have added atropine, Benadryl and Pethidine) antagonize the effect of acetylcholine on muscle, including the isolated auricles of the rabbit. Acetylcholine may play an important role in the maintenance of the body temperature and the adrenal gland may support this action, although the means by which this support is afforded is still unknown.

Report on Clinical Observations and Comment.

It is necessary to make some reservations when the results of animal experiment are used to explain clinical problems, but the experimental demonstration of pituitary regulation of thyroid and adrenal function suggests a possible cause for the maladaptation of catatonic patients to their thermal surroundings. Excessive vasoconstrictor reactions in these patients would hinder the response to chilling and muscular exercise if the blood supply were reduced not only in the skin but in other structures also; the full participation of the thyroid and pituitary glands might be prevented by the reduction of their blood supply.

Many patients observed here showed some of the physical signs usually associated with thyroid deficiency, such as thick, inelastic skin, coarse and sparse hair, a slow pulse and mental retardation. These signs were not limited to schizophrenics, but were present in many of their number. In a few cases of early catatonic illness the opposite features were observed, slight exophthalmos, rapid pulse and fine tremor of the hands.

Other signs of glandular deficiencies or imbalance were also noted. In chronic female schizophrenics (but in no male patients) pigmentation of the body-wall was often marked; the nipples of these cases were sometimes as dark as negroid skin. Hirsuties were common on the face and abdominal wall of female schizophrenics, who frequently showed a male type of body-hair distribution. The most striking physical change noted in about 5 to 10 per cent. of all catatonic patients, at some stage of their illness, was an asthenic syndrome, closely resembling the panhypopituitarism of Simmonds' disease. Physical improvement occurred in some of these cases after the onset of a mental remission, even when they had previously been considered "hopeless." This physical improvement has no counterpart in the organic illness. A low blood-pressure, amenorrhoea, wasting, asthenia, desiccated skin and atypical pigmentation were observed in cases in which these signs could not be ascribed to starvation; their food intake was often adequate, and wasting was not invariably present. There was no improvement in the state of their nutrition after overfeeding and when a gain in weight was obtained after a course of small daily doses of insulin there was often little change in the other somatic symptoms. Circulatory deficiency and asthenia point to a possible failure of adrenocortical activity, and the appreciable physical improvement which followed doca medication suggests that a disturbance of water and salt metabolism may play a part in the causation of this syndrome.

The difficulties of clinical interpretation are illustrated by the results of some objective tests which were applied to cases simulating simple glandular deficiencies. A cachectic catatonic woman, whose condition suggested adrenocortical deficiency and whose symptoms included extreme asthenia, amenorrhoea, a systolic blood-pressure of 70 mms. Hg, a pulse rate between 42 and 50 (but a normal low voltage electrocardiogram), a B.M.R. of minus 36 per cent., fair nutrition and marked pigmentation of the chest-wall, showed no evidence of adrenal failure when tested by Robinson, Power and Kepler's test (delayed excretion of additional intake of water), which gives a positive result in Addisonian patients (150). Hypoglycaemic unresponsiveness was present in 2 female catatonics and was absent in one male and one female catatonic who presented the same clinical picture. There was no obvious reason why this test should be positive in two of these patients, who showed a typical quick fall and a slow rise of the blood-sugar level after intravenous insulin administration. The insulin tolerance test, one of two tests devised by Russell Fraser and P. H. Smith (151) as objective criteria of panhypopituitarism and hypoadrenalism, was carried out according to these authors' instructions. Two positive results in a series of only 4 cases are obviously inconclusive, but they suggest the possibility of adrenal or pituitary dysfunction at some stage of a schizophrenic illness.

Selye's Alarm Reaction.

Selye described a polyglandular response to noxious stimuli and used this term in its widest sense to include exposure to cold and the consequences of muscular work. He published numerous studies on this subject and summarized his work in a recent publication (152). Shock or stress initiates this "alarm reaction," which is followed by an early adjustment named "counter-shock." This is succeeded, after prolonged exposure by a more permanent adjustment, a non-specific adaptation which confers resistance to further stress. The bodily changes observed in severe initial shock include hypothermia, hypotension, vasoconstriction, sweating, a low B.M.R., haemoconcentration, acidosis, immobility of the pupils and depression of the central nervous system or stupor; early leucopenia is followed by leucocytosis and a relative lymphopenia. This clinical description calls to mind some of the physical and mental changes which are observed in asthenic catatonics. During the process of adaptation the early signs of shock gradually disappear. Shrinking of the lymph nodes and thymus, which coincides with improvement, are attributed by Selye to increased activity of the cortex of the adrenal glands, secondary to secretion of adrenocorticotrophic hormone (A.C.T.H.). The alarm reaction was observed by Selye and his co-workers after many forms of stress, including oxygen deprivation, cold and muscular work, in the latter case without the initial stage of shock. When compensatory activity of the adrenal cortex is excessive or prolonged, lasting hypertension or other pathological changes may result. D. J. Ingle (153) has criticized Selye's interpretation of the alarm reaction, as he considers that a cortical deficiency may itself be a cause of damage to the organism and that this does not necessarily imply a failure to compensate for damage by other agents.

G. Sayers and M. S. Sayers (154) have observed an increased output of A.C.T.H. in experimental animals which are subjected to various forms of stress. The rate of pituitary secretion was found to be inversely proportional to the concentration of adrenocortical hormone in the tissues and the administration of cortical steroids suppressed adrenocortical activity by inhibiting pituitary secretion. Whereas physical exercise normally stimulates the growth of the adrenal cortex, it fails to do so when the function of the pituitary is inhibited by injection of adrenocortical extracts.

These experimental observations suggest new lines of approach to the problem of the catatonic failure of adaptation. Reasoning from analogy, the inadequate metabolic response of catatonic patients, after exposure to cold or to stresses imposed by muscular work, suggests a temporary pituitary or hypothalamic inadequacy with secondary thyroid and adrenal dysfunction. The absence of gross changes in endocrine glands is not surprising, as reversible reactions are characteristic of glandular activity and dysfunction may only indicate protracted activity or inactivity. Evidence is slowly accumulating to show that thyroid, adrenal and sex glands are subject to psychogenic stimulation which can raise or inhibit glandular function and can disrupt the concerted action of several glands. S. L. Simpson (155) remarked, in regard to another disturbance, psychological impotence, that the associated failure

of testosterone propionate, given in doses greater than those which are effective in complete castrates, seems to show that psychological processes may not only prevent an endocrine gland from functioning (as in anorexia nervosa), but can apparently prevent a hormone, which is present in supernormal concentrations, from acting on an end organ.

Recent experimental work has revealed that reactions to "stressful situations" include a fall in the lymphocyte count in both experimental animals and human subjects; a similar fall can also be induced by injection of extracts of functioning adrenal glands or of pituitary adrenotrophic hormone. F. Elmadjian and G. Pincus (156) observed the absence of a normal lymphopenic response in adrenalectomized animals after their exposure to cold surroundings or to continual disturbance; intermediate lymphocytic reactions occurred after one-sided adrenalectomy. The lymphocytic responses of normal males and that of 21 early psychotics, after exposure for 50 minutes to high environmental temperatures (40-44° C.), were compared by these authors (157). Normal subjects showed a 25 per cent. reduction in the lymphocyte count, while 20 of 21 psychotics showed a rise of approximately the same magnitude; a return to pre-stress level followed in all cases after 2 hours. H. Hoagland, F. Elmadjian and G. Pincus (158) also observed 6 normal persons, 2 schizophrenics and 1 psychopath during physical exercise, which was carried out in an atmosphere of lowered oxygen concentration; lymphopenic responses and increased excretion of 17-ketosteroids, related to the degree of stress, were noted in normal subjects, whereas the mental patients showed a rise in the lymphocyte count, unrelated to the degree of stress, and anomalous changes in ketosteroid excretion.

O. Diethelm, A. T. Milhorat and S. M. Small (159) found a rise in the total white count of psychotics who had experienced strong emotional disturbances of fear, anxiety and anger; up to 23,000 white cells were counted in schizophrenics and up to 15,000 white cells in agitated depressives. A subsequent intravenous injection of amytal caused the white-cell count to fall below the normal level. Earlier investigators often failed to distinguish between the various causes of "leucocytosis," such as haemoconcentration or reactions to infection, and their conclusions are therefore often contradictory. E. Goodall (160) found a moderate leucocytosis, with relative increases in neutrophil cells in early cases of dementia praecox, a relative lymphocytosis and a low total count in the later stages of the illness. Lymphocytosis also occurred in unfavourable cases of mania and in melancholia, "with the lapse of time."

Other physiological reactions linked to these lymphocytic responses are being gradually revealed by experimental work. The passage of lymphocytes from the glands into the circulation has been studied by T. F. Dougherty and A. White (161), who showed that corticosteroids oxygenated in position 11 initiate the dissolution of lymphocytes in lymphoid organs which results in hyperglobinaemia. The same changes were also observed after Roentgen radiation and were attributed by these authors to the direct effect of these rays on lymphoid tissue and stimulation of the pituitary gland (162). Adrenalectomy is followed by lymphocytosis owing to the failure of this mechanism of elimination.

J. M. Yoffey and J. S. Baxter (163) have observed a fall in the lymphocyte count after corticotrophin or adrenocortical extract injections into rats; prolonged medication with corticotrophin was followed by regressive changes in the lymph glands and thymus of these animals. G. Ungar (164) showed that the serum of traumatized animals inhibits histamine release from blood cells *in vitro*. He isolated a crystalline substance from splenic extracts which reproduced some of the secondary effects of the alarm reaction, namely reduction in bleeding time, increased capillary resistance and diminished histamine release *in vitro*. These adjustments to trauma were observed only in animals with intact spleens; in hypophysectomized or adrenalectomized animals they could be obtained after replacement-therapy with appropriate hormones. According to Ungar, "splenin A" is liberated by the spleen into the blood stream under pituitary-adrenal influence; it behaves like an anti-enzyme, protecting protein against the action of proteases which are freed by various traumatic agents (165). F. Elmadjian, H. Freeman and G. Pincus (166) have thrown light on the mechanism of these reactions by demonstrating a lymphopenic response in rats after the oral administration of sugar, the reaction being absent in animals subjected to adrenalectomy. In a recent paper G. Pincus, H. Hoagland, H. Freeman, F. Elmadjian and L. P. Romanoff (287) have described the response of schizophrenic patients to hyperglycaemia. They note that lymphocytopenia is less marked in these patients than in normal controls, but that the response to adrenocortical extract does not differ from that of the controls. Pincus and his colleagues conclude that schizophrenics suffer from a "species of adrenalism," a deficiency of adrenocortical secretion, but show no unresponsiveness to active corticosteroids, when these are administered in adequate quantities. These observations, and those of other workers who have noted the importance of hyperglycaemia in adaptation reactions to stress and trauma, suggest that Cannon's (167) emergency hyperglycaemia may initiate a pituitary-adrenal-splenic response. It is possible, but is still not proved, that hyperglycaemic blood stimulates the pituitary gland directly and causes an increased secretion of corticotrophic hormone.

Further work on abnormal responses to trauma must be awaited before the failure of any part of this complex mechanism can be claimed, but preliminary reports on the unusual lymphocytic responses of psychotic patients are sufficiently interesting to indicate the need for future investigation. If a remission is followed by a higher output of adrenocortical hormone, as is claimed by some observers, the coincident improvement in the physical condition may partly depend on an endocrine adjustment.

DISTURBANCES OF CARBOHYDRATE METABOLISM IN SCHIZOPHRENIC PATIENTS.

There is still lack of agreement on the nature of carbohydrate disturbances in psychotic patients and even on their occurrence. Although numerous studies dealing with this subject are reported in the literature, the conclusions drawn by different workers, who used similar methods of investigation on similar groups of patients, are often at variance. One of the obvious difficulties

is our ignorance of "normal" limits of variability under different external and internal environmental conditions. Another difficulty is the lack of information on the relative importance of various factors concerned in absorption and utilization of sugar, and our inability to control changes in the liver-threshold which result from the interplay of endocrine organs. Added complexity is introduced by the effect of normal and excessive emotional disturbances on some, if not all of these somatic processes. Among the welter of contradictory observations there are some statements which stand out in the literature, often repeated and seldom contradicted.

(1) The presence of a normal fasting blood-sugar level and the absence of a true diabetic blood-sugar curve, after oral glucose tolerance tests in the majority of psychotic patients.

(2) A tendency to sustained hyperglycaemia in patients suffering from mood disorders and in some schizophrenics, usually described as early or acute cases.

(3) A normal intravenous glucose tolerance test in many patients who show sustained hyperglycaemia after the oral administration of glucose.

This evidence suggests that some of the abnormalities of glucose metabolism in psychotic patients are related to altered absorption, or to an imbalance between the rate of absorption, storage and utilization of glucose. The high blood-sugar values encountered in some patients who suffer from mood disorders, suggest that emotional disturbances may sometimes be the cause of sustained hyperglycaemia after oral glucose tolerance tests (O.G.T.). Possible changes in intestinal absorption have received little attention since C. F. Cori (168) proved and H. E. Magee (169) confirmed, that in normal experimental animals absorption from the gastrointestinal tract is not subject to variation, even when the amount of sugar remaining in the gut is very small, and that the rate of absorption is constant for the species. There is, however, a considerable body of evidence to show that under altered circumstances, for instance, during starvation, or after epinephrine administration, the rate of absorption is modified, and in this case slowed. C. F. Cori (170) has himself noted that during the administration of small quantities of epinephrine, glucose absorption from the intestine of the rat is reduced, possibly as a result of slower evacuation of the stomach. W. O. Abbott, W. G. Karr, P. M. Glenn and R. Warren (171) observed that absorption from the duodenum of 4 normal female subjects, after temporary occlusion of the duodenojejunal junction by a balloon, varied from day to day. Although this method of estimating the rate of absorption is open to objection, daily variations of the amount of glucose left in the duodenum are difficult to explain, except by a change in the rate of absorption. B. H. Balser and B. L. Pacella (172) have also noted that the O.G.T. curve of personnel subjected to operational fatigue was flat in 38 per cent. of the cases investigated, whereas intravenous glucose tolerance tests were perfectly normal in the same subjects, a difference which could be explained by reduced absorption from the gastrointestinal tract. A flat O.G.T. curve and normal absorption of fructose is a common occurrence in cases suffering from sprue, and may point to the failure of phosphorylation, necessary for the absorption of glucose,

whereas diffusion of fructose remains unaltered (B. G. Macgrath *et al.* (173)).

Sustained hyperglycaemic levels after O.G.T. tests have been recorded most frequently in depressive and manic-depressive patients, but a few observers have noted similar sustained blood-sugar levels in stuporous dementia praecox patients (S. A. Mann (174)). T. Raphael and J. P. Parsons (175) are of the opinion that the O.G.T. curves of dementia praecox and depressive patients are characteristic and differ strikingly from each other and from those of normal controls. Depressive patients, according to these observers, show an initial hyperglycaemia with a high rise of the blood-sugar level and fail to return to their fasting level after 2 hours. Dementia praecox patients show greater variability; the rise of the blood-sugar level is usually rapid, but return to the low initial level is often delayed, and individual variations in the height of the O.G.T. curve are marked. P. K. McCowan and J. H. Quastel (176) have found sustained hyperglycaemic levels in many psychotics after oral ingestion of glucose, and have expressed this abnormality by means of a mathematical formula. The calculated hyperglycaemic index of these patients was found to vary with the degree of emotional tension, rather than with the type of mental illness from which the patient suffered.

A "lag storage" blood-sugar curve, first described by H. MacLean (177), is discussed by R. D. Lawrence (178), who prefers to call it a "steeple curve." It resembles the high-peaked "schizophrenic curve" of T. Raphael and J. P. Parsons (175), but shows no protracted hyperglycaemia: an early peak precedes a quick return to fasting level. This curve is common after gastro-enterostomy, and in patients suffering from duodenal ulcer, but is also found in some normal subjects after rapid absorption of sugar from the intestine. A similar curve with temporary hyperglycaemia and glycosuria can be induced by introducing sugar into the duodenum after intubation, while the same amount of glucose taken orally will show a normal curve. Flooding with sugar in the first case prevented the storage mechanism from keeping pace with the volume of sugar absorbed. G. D. Greville (179) has drawn attention to the importance of intestinal absorption as a cause of alteration in the O.G.T. curve; he observed that the slower the initial rate of rise the more sustained the level of hyperglycaemia. The initial slope of the O.G.T. curve is, according to Greville, an indication of the rate of glucose absorption; it is correlated with the time taken by iodide, ingested as potassium iodide, to be secreted in the saliva.

There is general agreement that a flat O.G.T. curve may result from diminished absorption of glucose, but sustained hyperglycaemia is not usually ascribed to increased absorption, the blood-sugar level being controlled by a storage reaction. H. MacLean and O. L. V. de Wesselow (180) have, however, noted that although the curve is not raised by a second administration of oral glucose during the stage of absorption, hyperglycaemia is prolonged beyond the 2nd or 3rd hour by repeated ingestion of glucose. It is possible that slowed absorption has the same effect on the blood-sugar curve as repeated ingestion, and that this delay may account for sustained hyperglycaemia in some cases.

S. Soskin and R. Levine (181) have reviewed the whole subject of carbo-

hydrate metabolism. They came to the conclusion that the liver is of the greatest importance in the regulation of the blood-sugar level, a fact which was well known to Claude Bernard, but which has been forgotten by some later observers. The threshold for glycogenolysis is set by the balanced action of endocrine glands; epinephrine and insulin, respectively raise or lower the glycolytic function of the liver (C. F. Cori (170)).

Increased resistance to insulin has been suggested as a cause of sustained hyperglycaemia in schizophrenic patients. There is agreement that insulin resistance is frequent in schizophrenia and that changes in sensitivity commonly occur during the course of insulin treatment. H. Freeman, J. M. Looney, R. G. Hoskins and C. G. Dyer (182) have found that insulin resistance was present in 41 per cent. of 32 schizophrenics tested by them, while M. M. Harris (183) has noted both increased and decreased sensitivity to test doses of insulin in schizophrenic patients; the sera of a group of 7 of these patients proved to be antagonistic to insulin when tested by biological assay.

The occurrence of persistent hypoglycaemia after intravenous insulin administration, so-called hypoglycaemic unresponsiveness, is considered by Russell Fraser (151) to be objective evidence of panhypopituitarism, hyperinsulinism or hypoadrenocorticalism. It is possible that the occurrence of insulin sensitivity in some schizophrenic patients may also result from a glandular disturbance. S. P. Colowick, G. T. Cori and M. W. Slein (184) have shown that the point of action of anterior pituitary hormone and insulin is hexokinase which catalyses the transfer of the phosphoric acid group from adenosine triphosphate to glucose. Hexokinase is inhibited *in vitro* by anterior pituitary extract (and by certain adrenal steroids) and this inhibition can be released by the addition of insulin. This is not the only action of insulin, as hypophysectomized animals are very sensitive to this hormone, but it explains one of the possible mechanisms of pituitary-insulin antagonism and varying insulin sensitivity.

C. F. Cori (170) has pointed out that the pancreas is undisturbed by elimination of its vagal supply by the administration of atropine, whereas denervation of the adrenal glands prevents the discharge of adrenalin in response to hypoglycaemia. Secretion of adrenalin may be the starting point of the chain of somatic events which determine a sustained hyperglycaemic response in patients suffering from affective disturbances. Adrenalin provokes hyperglycaemia and among other actions stimulates the adrenal cortex and slows absorption from the intestinal tract; it is evident that it may modify the blood-sugar level in one of many ways.

The changes introduced by altered intestinal motility and absorption are eliminated by intravenous injection of sugar. It has been recognized by many observers that the intravenous glucose tolerance curve of psychotics shows fewer abnormalities than their O.G.T. curve. This conclusion was reached by J. C. Thomas, B. Gilsenan and E. J. C. Hewitt (185) who found, however, that the response to intravenous glucose, insulin and adrenalin gave evidence of persistent hyperglycaemia, insulin resistance and raised adrenalin sensitivity in 10 of 20 schizophrenics. They attributed these changes to a possible endocrine disturbance.

The carbohydrate metabolism of psychotics has been reviewed by H. Holmgren and S. Wohlfahrt (186) ; these authors have concluded from their own work, and that of others, that phasic hyperglycaemic levels are a common disturbance in manic-depressive illness and in the acute stages of schizophrenia. Dieting and restlessness were found to have little effect on the shape of the O.G.T. curve, but the degree of affective disturbance was found to be of great importance ; the blood-sugar curve reflected the " Stärke des Gefühls," in the Kretschmerian sense (Höhe-Dauer-Aeusserung). These authors agree with R. A. McFarland and H. Goldstein (187) that great inter- and intra-individual variability distinguishes the schizophrenic response to various tests, a sign, in their opinion, of defective homeostasis and maladjustment to environmental stresses. They found evidence of endocrine disturbances in most psychotics, and ketonuria only in schizophrenic patients. High fasting blood-sugar levels were more frequently present in patients of pyknic type than in those with a different physique. Holmgren and Wohlfahrt employed a new test of carbohydrate metabolism, noting the effect of two-hourly injections of epinephrine on the blood-sugar level of normal and psychotic persons, during a 24 hours' fast. Gradual sinking of the blood-sugar level was the rule in the normal subjects, but a rise was noted in psychotics who suffered from a severe affective disturbance ; the rise, when it occurred, was unrelated to the type of mental illness from which the patient suffered. Improvement after E.C.T. was evidenced by lowered sensitivity to adrenalin, the fasting blood-sugar curve now resembling that of a normal person.

K. M. Bowman and J. Kasanin (188) have observed the effect of emotional disturbance on the blood-sugar level of 148 mental patients who suffered from various mental illnesses ; they failed to find any correlation between the moods of these patients (with the possible exception of excitement) and the height of their blood-sugar curve. O. Diethelm (189), on the contrary, believes that the changes of the O.G.T. curve are characteristic of various affective states. Although a rise of the blood-sugar level is common to all cases of acute anxiety, tension or fear, a high early peak is considered by him to denote rapid absorption of sugar during acute anxiety, whereas less acute tension may result in sustained hyperglycaemia. The difficulty of distinguishing between kinds and degrees of emotion may deter others from following Diethelm's attempt to interpret the O.G.T. curve in terms of our present knowledge of emotional experience.

Report on Clinical Observations and Comments.

A few observations on the carbohydrate and fat metabolism of patients investigated here are appended.

Acetonuria.

The most striking metabolic disturbance of catatonic patients was their liability to attacks of acetonuria, which were unaccompanied by hyperglycaemia or glycosuria. The nutrition of some of these patients was fair ; they were not suffering from starvation as they were ingesting food in adequate quantities, but they required large supplements of glucose (in one case as much

as 8 ounces daily), in addition to a diet rich in carbohydrates, before acetone could be temporarily eliminated from the urine. Small daily doses of insulin helped to reduce ketonuria in these patients. Acetone is often present in the urine of newly admitted cases of mental illness and it is customary to ascribe its presence to starvation, although the history may not suggest refusal of food. It is possible that inability to absorb, store or use ingested glucose, resulting from an endocrine disturbance, causes a swing towards increased fat metabolism. The beneficial effects of small daily doses of insulin suggests that this may be the correct interpretation.

Glucose Tolerance Tests.

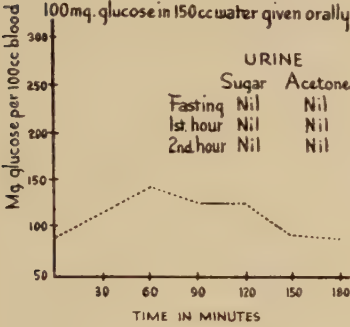
Repeated oral glucose tolerance tests were carried out on 35 schizophrenic patients of both sexes, most of them early cases showing catatonic or paranoid syndromes, and a few hebephrenics. These patients were repeatedly tested over a period of 6 to 18 months, 3 to 10 tests being carried out on each patient, at intervals of one or more weeks. The capillary blood sugar was estimated half-hourly for 3 hours, by Jenson and Hagedorn's method, after ingestion of 50 or 100 grams of glucose, following a 12 hours' fast. A low normal fasting blood-sugar level of 70-80 mgm. glucose in 100 ml. blood and a low curve were the rule in these schizophrenics; only 5 patients showed a persistent tendency to sustained hyperglycaemia, and of these, 3 suffered from slight exophthalmos.

Ten depressive psychotics were used as controls; they showed a higher and more sustained hyperglycaemic level in response to the O.G.T. test and a slightly higher, but still normal, fasting blood-sugar level (90-110 mgm. glucose in 100 ml. blood). Intravenous sugar tolerance tests were carried out on 10 schizophrenics and 5 depressives, by R. M. McKean, G. B. Myers and E. C. Von der Heide's technique (190). In 10 of these cases the blood-sugar curve was perfectly normal, while in 5 others (3 schizophrenics and 2 depressives) slightly raised 15 minutes' readings were obtained between 125 and 150 mgm. glucose in 100 ml. blood (normal value stated to be below 125 mgm. in 100 ml.).

It soon became evident that all the known factors, including changes in absorption and changes in mood, would have to be taken into consideration when attempting to interpret an "abnormal" O.G.T. curve. It was found possible, for instance, to modify the shape of the curve by varying the speed of sugar ingestion in direct duodenal feeding. Four male catatonics having volunteered for intubation, a Miller-Abbott tube was passed into their duodenum, the change in the reaction of the juice withdrawn from the tube being taken as a guide to its entry into the small intestine. A glucose feed was poured in quickly (100 g. glucose in 150 c.c. water, in 4 min.); this resulted in a quick rise of the blood-sugar level and a rapid return to fasting value. Slower administration of the same amount of glucose, given at an even rate over 90 min., in an attempt to imitate the slow passage of sugar from the stomach into the duodenum, caused a slower rise in the O.G.T. curve and more sustained hyperglycaemia, with a delayed fall to fasting level (Chart III). The same tests were carried out on 3 female depressives; there was little difference between the results of quick and slow feeding in these 3 patients and almost

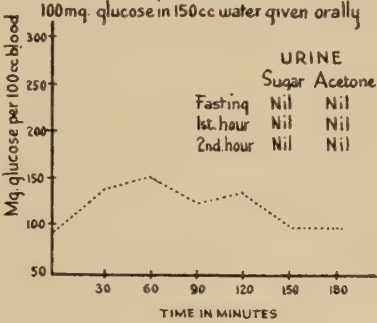
MALE SCHIZOPHRENIC AGED 26

Pt. A O.G.T. Date 9-7-45



MALE SCHIZOPHRENIC AGED 34

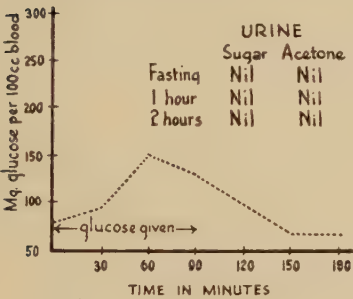
Pt. B O.G.T. Date 9-7-45



SLOW DUODENAL FEED

Pt. A Date 3-7-45

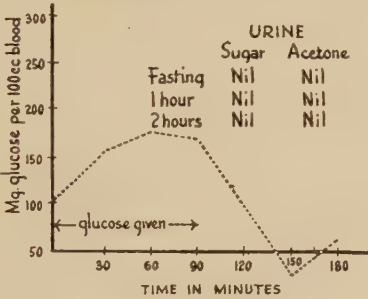
100mg. glucose in 150cc water poured into small intestine at even rate in 90 mins. through a Miller-Abbott tube.



SLOW DUODENAL FEED

Pt. B Date 3-7-45

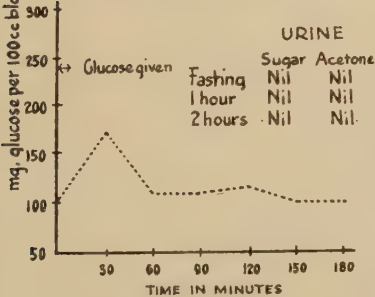
100mg. glucose in 150cc water poured into small intestine at even rate in 90 mins. through a Miller-Abbott tube.



QUICK DUODENAL FEED

Pt. A. Date 1-7-45

100 mg glucose in 150 cc. water poured into small intestine at even rate in 4 mins. through a Miller-Abbott tube.



QUICK DUODENAL FEED

Pt. B. Date 1-7-45

100 mg. glucose in 150cc water poured into small intestine at even rate in 4 mins. through a Miller-Abbott tube.

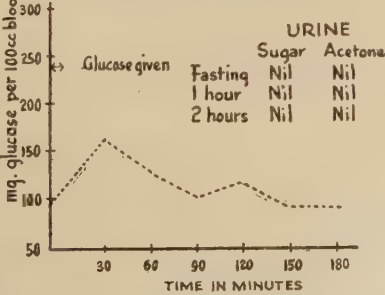


CHART 3.

equal sustained hyperglycaemic curves, with a delayed return to fasting blood-sugar level were observed in all cases. It seems probable that the effects of emotional disturbance may outweigh and mask any change introduced by different rates of absorption. The effects of emotional disturbance were striking in the case of depressive patients, causing an unusually sustained curve which could be predicted or even induced, by any circumstance which increased a patient's anxiety. A suggestion that a change of ward would be necessary, or preparations for a subsequent dressing, would cause the O.G.T. curve to rise continually for three hours or longer. Simultaneous signs of agitation, wide pupils and a rapid pulse gave evidence of increased sympathetico-adrenal activity. The low O.G.T. curve of the schizophrenic patients was not raised by events which were likely to cause affective disturbances in others, nor did any constant changes in the curve follow physical treatment, evolution of the psychosis, mental improvement or relapse. Five schizophrenics, 3 of whom showed slight exophthalmos, gave exceptionally high curves; very low curves were obtained from asthenic catatonics who clinically resembled cases of Simmonds' disease. These were the only notable exceptions among the schizophrenics; it is possible that hyper- and hypo-activity of the pituitary, with associated changes in the rate of absorption, storage and utilization of sugar are responsible for these slight deviations from normal glucose tolerance.

The result of these tests gave no indication of gross errors of carbohydrate metabolism in the 35 schizophrenics who were investigated. It is suggested that, taken in conjunction with the evidence previously reviewed, they are consistent with the following suppositions:

(1) Sustained hyperglycaemic curves may result from changes in the rate of absorption; they follow prolonged and therefore probably slowed absorption. A slow rise in the curve usually precedes sustained hyperglycaemia; the trigger storage mechanism may fail, when the blood sugar is raised slowly, or storage and tissue consumption may be adversely affected by endocrine factors which delay absorption.

(2) Hyperglycaemia may be caused and maintained by somatic changes evoked by emotional disturbance. These changes are probably governed by increased adrenalin secretion and by secondary effects to which this gives rise. Depressive patients, but not schizophrenics, showed changes in the O.G.T. curve which were accentuated by increased emotional disturbance.

(3) An endocrine dysfunction is suggested by a very flat or by a sustained hyperglycaemic curve in schizophrenic patients who show other somatic evidence of endocrine dysfunction.

DISTURBANCES OF SEXUAL FUNCTION IN SCHIZOPHRENIA.

Histological changes in the structure of the male glands were reported in early studies of Sir Frederick Mott: these changes were mainly interstitial and could have resulted, according to other observers, from an intercurrent or terminal illness. Interest has been revived by the finding of tubular atrophy in the testes of schizophrenic patients examined by testicular biopsy. R. E.

Hemphill, M. Reiss and A. L. Taylor (191) have described advanced tubular changes, hyalinization of the basement membrane and degeneration of testicular elements in over 50 per cent. of 90 schizophrenic males they examined; the change was most marked in deteriorated chronic cases, but was also evident in some of the youngest patients, whereas paranoid schizophrenics were usually immune. No correlation was found between the degree of testicular atrophy and the excretion of 17-ketosteroids.

Irregularity of the menstrual cycle and long periods of amenorrhoea are common in female psychotics, particularly in schizophrenics, and they have sometimes been attributed to a primary change in the function or structure of the ovaries. Support for this theory has been sought in statistical evidence of reduced fertility. F. J. Kallman (192) considers this reduction to be important in catatonic and hebephrenic patients, but not in paranoid schizophrenics.

One of the easiest means of assessing cyclical changes of ovarian function is a daily record of body temperature; the regular biphasic change in a temperature chart, which covers the whole menstrual cycle, is accepted as evidence of regular ovulation (P. Tompkins (193)). Unfortunately this simple test is seldom applicable to schizophrenics, their body temperature showing irregular independent swings which are unrelated to any known somatic disturbance. Suppression of menstrual function following minor psychogenic disturbances is such a common occurrence that amenorrhoea cannot, in itself, be regarded as evidence of major ovarian dysfunction. Amenorrhoea lasting some months or years has been reported after "emotional storms," by A. Bourne (194), and after unhappiness or frustration during internment, by A. Sydenham (195), etc. The schizophrenic disturbance is usually of greater duration and in this respect resembles the amenorrhoea of anorexia nervosa, or of Simmonds' disease; in all three conditions it occurs early and it has been observed in anorexia before malnutrition has become marked (J. A. Ryle (196)).

If published work is a guide to the number of investigations into the structure and function of the gonads of female schizophrenics, it must be concluded that the subject has been neglected and that little information is yet available.

A change in the balance of female sex hormones has been held by some observers to explain Raynaud-like syndromes in female patients. A. G. M. Raynaud (197) himself reported the disappearance of local syncope as a first index of pregnancy in one of his patients. P. M. F. Bishop (198) believes acrocyanosis to be the result of ovarian deficiency, alleviated by oestrogen therapy, and D. I. Abramson *et al* (199) has noted the improvement of the peripheral circulation after stilboestrol therapy.

In experimental animals E. J. G. McGrath (200) has observed that theelin can protect these animals from developing gangrene of the tail after injection of ergotamine tartrate. It was later shown by M. M. Suzman, C. C. Freed and J. J. Prag (201) that castrated male rats were similarly protected by the addition of this hormone. S. R. M. Reynolds (202) proved that oestrogen causes local liberation of acetylcholine in the uterine tissue of experimental animals, a circumstance which may explain its vasodilator action on the blood vessels

of other tissues. E. J. McGrath and L. C. Herrmann (203) treated 345 patients who suffered from vasomotor disturbance with oestrogen, and reported definite improvement in the peripheral circulation, whereas J. C. White and R. H. Smithwick (204) deny the beneficial effects of oestrogen therapy in vasospasm. F. J. Browne (205) has reviewed the evidence for pre-eclamptic sensitization of the arterioles and has come to the conclusion that chorionic gonadotrophin, rather than oestrogen, sensitizes the vascular system to pressor hormone. Oestrogen has been claimed as a sensitizer by other observers.

It is not excluded that the water-retaining properties of the sex hormones may account for their beneficial effects on the circulation. Contradictory findings, such as sensitization of the blood vessels by gonadotrophin and oestrogen, and improvement of the local circulation by oestrogen or stilboestrol, would be difficult to reconcile if local mechanisms alone were considered. The whole subject requires further investigation and in the present state of our knowledge the prevalence of vasospastic conditions among female schizophrenics cannot be attributed, without further proof, to lack of oestrogen secretion in these patients.

Report on Clinical Observations and Comment.

An attempt was made to investigate the function of the gonads of some female schizophrenic patients of this hospital. The early morning rectal temperature of 4 young catatonics who had had irregular and scanty menstrual periods for some months was recorded daily over a period of three months. These records showed only irregular rises of temperature, which started from a low basal level (97-98° F.) and could not be explained by regular cyclical changes, or obvious deviations from good health. These irregular rises were therefore ascribed to excessive heat regulating reactions, as peripheral vasoconstriction seemed to give support to this theory.

A more promising clinical guide to ovarian activity was found in a study of the vaginal mucous membrane, as suggested by the work of G. N. Papanicolaou (206). Repeated smears of the vaginal mucous membrane were taken from 30 female schizophrenics, 13 depressives and 13 normal controls, all between the ages of 25 and 40. Twin sets of slides were stained, using haematoxylin and iodine vapour, as suggested by H. C. Mack (207). These smears showed that cornification of the vaginal epithelium was defective in many of the psychotics examined, more especially in the schizophrenics. In the majority of schizophrenics (approximately two-thirds of the patients investigated) the vaginal epithelial cells were much smaller than those found in the normal controls of the same age. They were rounded instead of squamous and glycopenia was very marked. These vaginal smears resemble those described by H. C. Mack as showing advanced stages of ovarian dysfunction. They correspond to grade I and grade II oestrogen deficiency of Mack's classification (normal smears are grade IV), and their appearance is often identical with that of the "atrophic menopausal type" described by G. N. Papanicolaou and E. Shorr (208). Glycogen was grossly deficient in many cases and was completely absent in 4 of the 30 schizophrenics. In patients with an atrophic mucous membrane and poor glycogen cell-content, amenor-

rhoea was the rule. The shape of the cells of the mucous membrane of 13 depressive patients resembled more nearly that of the 13 normal controls, but the size, cornification and glycogen-content of these cells showed a definite reduction in about one-third of the affective patients examined. Only one of the "normal controls," a woman who was admitted to a neighbouring hospital for a minor operation, showed an epithelial picture similar to that seen in the majority of schizophrenic patients; on further enquiry it was found that this woman suffered from dysmenorrhoea and sterility. The possibility that oestrogen deficiency in schizophrenic patients is secondary to pituitary dysfunction, the result of deficient gonadotrophic secretion is suggested by other signs of polyglandular disturbance in these patients, and by their resemblance to cases of panhypopituitarism.

The action of carbon dioxide inhalation, restoring, within a few days, the menstrual function of 10 of 18 schizophrenic patients, whose amenorrhoea had lasted from 7 months to 4 years, has already been noted. Eight of these ten patients are known to have had a second, or a second and third menstrual period, without further carbon dioxide inhalations, before the cycle was again interrupted. Re-establishment of the periodic function suggests a central action, possibly related to the vasodilator effect of carbon dioxide on the cerebral vessels.

Parenteral corticotrophin, given to 4 catatonic women for 7 consecutive days or longer (Cortrophin Organon, 5 units), caused little if any change in the appearance of the vaginal mucous membrane; vaginal changes after carbon dioxide inhalations were also inconclusive.

DYSFUNCTION AT THE HYPOTHALAMIC LEVEL AND DISTURBANCE OF MENTAL AWARENESS IN SCHIZOPHRENIC PATIENTS.

Experimental work on the hypothalamus has shown that the higher centres of autonomic integration are grouped in this and in adjoining areas of the brain. The observation of P. Bard (209) that sham rage in cats followed division of the brain stem, when the section was made above the mid-diencephalic level, and the experimental work of Goltz, Dusser de Barenne, Ranson and others have encouraged the belief that conscious emotional disturbances may be experienced at this level of the central nervous system; Bard, however, was careful to avoid this conclusion. He stated plainly that it was "reasonable to suppose that the neurological processes which underlie emotional consciousness are cortical." Later experimental work by J. Masserman (210) has confirmed this supposition. Masserman found no evidence of affective experience after direct stimulation of the hypothalamus in experimental unanaesthetized animals; he obtained only motor manifestations which were characteristic of fear and rage, such as snarling, lashing, mydriasis and pilo-erection. These outbursts were diminished by the administration of barbiturates and were increased by picrotoxin and metrazol; they were always undirected and unadapted to circumstance: the animals dashed their heads against a wall in their effort to escape, and when they failed to do so they proceeded to purr and lap contentedly. Conditioned reflexes cannot be established by hypo-

thalamic stimulation and learning from experience is never observed. After extensive hypothalamic lesions somnolence, catalepsy and stupor are common, as well as depression of the general metabolic level. Masserman concluded from his experimental work that the hypothalamus integrates and possibly reinforces the effector impulses which control the sympathetic and motor manifestations of fear and rage, but that discharges which are obtained by hypothalamic stimulation do not modify the spontaneous emotional behaviour of an animal. W. R. Hess (211), who worked with animals which had not been decorticated, found that hypothalamic stimulation caused aggressive behaviour which was purposeful and was usually directed against the nearest person.

T. V. Moore (212) considers that Masserman has gone too far in excluding the hypothalamus as a "locus of emotional experience." The work of H. Cantril and W. A. Hunt (213) with adrenalin, and that of R. R. Grinker and H. Serota (214) on stimulation of the human hypothalamus with electrodes placed in the sphenoid bone, show that affective disturbances may follow thalamic stimulation, anxiety being experienced in both cases. Moore, who considers that these experimental results suggest conscious thalamic experience, distinguishes between physiological affective experience and that related to emotion; the latter is regarded by him as the psychic reaction to conscious evaluation of the predicament in which the animal is involved. He believes that stimulation of the hypothalamus may lead not only to exaggerated emotional responses but also to intensified affective experience. Sir Henry Head's clinical observation that hyperhedonic experience may result from lesions which irritate the thalamus or free it from cortical inhibition is quoted by Moore in support of his views.

The clinical syndromes observed in some patients who suffer from cerebral trauma, new growths, or post-encephalitic involvement of the hypothalamus, are proof that behaviour may be modified by interference with hypothalamic function; B. J. Alpers (215) considers that the subjective sensation known as "affect" may be altered by disease of the hypothalamus. Maniacal manifestations have frequently been recorded during surgical manipulation of the anterior hypothalamus and forced smiling, laughing and crying occur in patients who suffer from disseminated sclerosis, in which periventricular lesions are common. Meaningless laughter is common also in catatonic schizophrenics; it is usually regarded as evidence of incongruous affect in these patients, but clinical observation suggests that their laughter is sometimes involuntary, a release of tension rather than an expression of emotional experience.

The reasons which have been adduced in favour of hypothalamic dysfunction in schizophrenia are manifold. The hypothalamus being a centre of autonomic integration, compensatory changes in body function, particularly the vascular disturbances associated with a fall in the general metabolic level, are dependent on hypothalamic control. The polyglandular nature of a schizophrenic endocrine disturbance suggests a possible defect of hypothalamic function. Some of the somatic manifestations of schizophrenia, postural rigidity, and occasional sialorrhoea, are not unlike those observed in encephalitis lethargica, in which the lesions are situated in areas adjoining the hypothalamus.

These considerations have suggested that the somatic manifestations of schizophrenia may be related to a disturbance of the hypothalamus.

As the schizophrenic disturbance is reversible, the absence of structural defects in the central nervous system, or in the glandular organs, is not surprising and does not exclude hypothalamic dysfunction. It is, however, improbable, in view of other considerations, that the hypothalamus is primarily at fault. The body functions which are controlled by the hypothalamus being subject to psychogenic stimulation, the somatic manifestations of schizophrenia may result from a disturbance at a higher level of the central nervous system.

Disturbances of Posture and Movement in Catatonia.

Various experimental studies and observation of allied pathological states have thrown some light on the disturbances of posture and movement which occur in catatonic patients.

Ranson and his collaborators (216) have noted that—in cats—electro-coagulation of the boundary zone between the hypothalamus and the midbrain was followed by cataleptic reactions, plastic tonus of the muscles, a lack of motor initiative and subnormal emotional expression which resemble the physical manifestations of catatonia. The counterpart of this syndrome is cataplexy, in which relaxation of the musculature causes a sudden slumping of the body; it has been likened to the postural component of sleep, except that it usually follows a sudden emotional disturbance in a predisposed person.

Experimental catalepsy has attracted the attention of many workers (H. H. de Jong (97), A. van Harreveld and D. J. Kok (217), etc.). It has been produced by a multiplicity of physical agents, among which deprivation of oxygen and intoxication with various drugs have played a part, but we are no nearer to understanding the underlying neurological mechanism or the common feature shared by these physical agents. Ranson's experimental evidence suggests that their action may be exerted on a hypothalamic centre.

The physical manifestations of catatonia show some points of similarity with Parkinsonian akinesia and rigidity. These are as a rule much less transient, but they can be modified by psychogenic factors and it has long been known that Parkinsonian rigidity may be altered during the course of impulsive action. A striking demonstration of this ability to perform quick and agile movements under special circumstances, was given by a group of post-encephalitic patients under Dr. Brander's care, at a meeting of the Royal Society of Medicine at Friern Mental Hospital. These patients showed typical rigidity before they commenced a display of physical exercises; as their competitive fervour was aroused their limbs became supple, and at the height of excitement they performed movements of great agility. They stiffened again as soon as the performance ended and a few minutes after turning cartwheels had to be taken to their wards on trolleys, as they were now unable to walk.

Relief of static rigidity (the *Stutzreaktion* of A. van Harreveld and D. J. Kok (217)) by an emotional reaction, recalls the occasional termination of catatonic rigidity and negativism in response to affective stimuli. An instance of this reaction was observed here in a young girl who had resisted all induce-

ments to terminate a stuporous episode and was aroused by overhearing that a mistress she had admired had previously been a patient in a mental hospital. The girl's expression and posture instantaneously changed from strained catatonic immobility to normal relaxed features, and she was able to walk briskly from the room into which she had previously had to be pushed. When questioned about this change she showed complete lack of insight, the nearest approach to an explanation being her answer, "It was time I pulled myself together." The instance was remarkable, as this girl had deteriorated for over a year and after this event she progressed to a complete remission and was later able to undertake a course of professional training.

The opposite occurrence is only too familiar, a sudden sinking into stuporous akinesia, following an apparently trivial physical or mental event. During a study of word association, a young catatonic woman who had a very bad family history (three of her near relatives were detained in mental hospitals) was observed to sink into stupor whenever an item in the test referred even distantly to her personal and matrimonial troubles. According to the emotional value of the key word, she would either pause, refuse to associate, or withdraw into stupor. Her limbs became rigid, her features set and distorted by frequent attacks of forced laughter. She also showed remarkable dissociation of ocular movements, which is discussed later. On some occasions there was marked slowing of the pulse and a fall of blood pressure with peripheral cyanosis. It was found that the development of this stuporous reaction could be cut short by carbon dioxide inhalation, and that her withdrawal was less likely to occur after the preliminary administration of Benzedrine. When this patient escaped into stupor, her recall was sometimes made possible by coaxing, reassurance, or repeated pressing demands, but as her mental condition deteriorated during the second and third years of hospitalization she became a typical catatonic schizophrenic with few clear periods. She failed to respond to insulin treatment and in the later stages of her illness she could only be roused for brief periods by an electrically induced convulsion.

We possess no direct evidence to explain the processes which tilt the unstable mental balance in catatonia. Comparison with somewhat similar physical changes in experimental catalepsy and Parkinsonian illness (such as rigidity and akinesia) suggests that physiological changes at the hypothalamic level may account for some of the physical components of the catatonic reaction.

Disturbances of Consciousness in Catatonia.

The changes in mental awareness in catatonia are as striking and as difficult to explain as the physical changes observed in this illness. A diminution of mental awareness, particularly when the thought processes show a dream-like quality, have suggested a likeness to the mental changes which occur during sleep, and therefore a possible disturbance of the "sleep-centre," the mechanism which permits wakefulness.

Disturbances of this mechanism form the subject of numerous clinical and experimental studies, amongst which clinical observations by C. Davidson and E. L. Demuth (218, 219 and 220) and experimental work by S. W. Ranson and H. W. Magoun (111), W. J. H. Nauta (221) and N. Kleitman (222) are perhaps

the most notable. Catatonic stupor has, however, very little in common with the features of normal or pathological sleep. Sleep is as a rule normal in catatonia and *flexibilitas cerea*, akinesia and peripheral vascular changes are relieved by the onset of sleep. This has been noted, and recorded photographically, by T. W. Forbes (223) and other observers; catatonia should therefore be considered a disorder of the state of wakefulness rather than of sleep.

The work of N. Kleitman led him to consider a subdivision of consciousness into consciousness of choice and consciousness of necessity. If this subdivision is accepted, one may perhaps regard the diminished awareness of stuporous catatonics as an impairment of the consciousness of choice. Higher mental processes are only possible when cortical function is both fully developed and functionally efficient, and they are absent when the cortex is either immature or when it has been damaged by such physical agents as hypoxia, trauma infection or intoxication. Disturbances of consciousness induced by mescaline intoxication resemble schizophrenic dissociation in that the changes of critical awareness which they induce do not amount to a loss of consciousness, differ from sleep, and entail a disturbance of thought processes, reality feeling and orientation in time. Florid hallucinatory experiences and a lack of insight complete the schizophrenic colouring of this experimental psychosis (M. Critchley (224), G. T. Stockings (225)).

Thought disturbances similar to those experienced by schizophrenic patients, may be observed in some patients who suffer from an organic mental illness; it has been suggested that a physical change and a loss of integrity of structure or function of cerebral tissue may account for the changes in mental awareness and for altered thought processes in schizophrenic patients. H. D. Singer (226) considers that a psychotic illness follows a structural change of the central machinery of autonomic integration. Adjustment to this disturbance varies with the personality of the patient and determines the form taken by the psychosis; it may result in one or other mental illness, neurasthenic, depressive, manic, schizophrenic, etc. Singer's concept of mental illness is still mainly theoretical. If evidence of a central disturbance becomes available, a functional psychosis will then presumably be found to depend on a functional and reversible change of this central mechanism. In schizophrenic catatonic disturbances of awareness the mental and physical changes are essentially reversible, as shown by the multiplicity of curative agents which can produce a temporary improvement. A fleeting improvement may also follow an adequate mental stimulus, such as a command, entreaty or chance word, the significance of which is personal and charged with affective meaning. Arousal from stupor by a selective psychogenic stimulus is a process comparable to interruption of normal sleep by a physically inadequate stimulus, such as the wail of an infant, which may arouse a woman who has slept through a bombardment. This comparison suggests that in both catatonic stupor and in sleep, the physical and mental faculties are only in abeyance and can be recalled by an appropriate stimulus.

Experimental evidence has shown that the activity of the highest centres of the brain is altered by extinction of the thalamic centres. According to

S. Obrador (227), rhythmic electrical activity of the cortex of the brain can be abolished by destruction of the hypothalamus, but F. Bremer (288) has recorded rhythmic cortical activity after division of the mesencephalon or complete isolation of a part of the cortex. K. Kristiansen and G. Courtois (289) agree with Bremer that the cortex is not silent after its isolation, and that the response to chemical stimulation of an isolated part of the cortex is very similar to that of the normal brain. Bremer and Kristiansen both believe that this rhythmic electrical activity is an inherent property of the grey matter of the cortex and that it is not necessarily dependent on an intact cortico-thalamic circuit. As cortical silence is not an invariable sequel to destruction of the thalamus, suppression of cortical electrical activity may perhaps result from accidental anoxia or vascular deprivation of the brain. The origin of cortical rhythms cannot be regarded as finally settled, but most observers agree that, whether the cortex initiates its own rhythmic activity or is driven by a lower centre, cortical activity is modified by the activity of centres situated at a lower physiological level. H. H. Jasper and J. Droogleever-Fortuyn (290) were able to demonstrate the influence of thalamic intralaminar systems on the rhythmical activity of the cortex of experimental animals. Clinical evidence suggests that changes in the electrical activity of the cortex may result from lesions of the diencephalon (W. Grey Walter, G. M. Griffiths and S. Nevin (228)). W. Grey Walter is of the opinion that the hypothalamus may be responsible for initiating and/or, maintaining some, but not all, of the spontaneous scanning rhythms, which translate sensations, apparitions and images via conscious symbols, into effector behaviour (personal communication). Other evidence points to the fact that normal mental awareness is only possible when the hypothalamus is intact. H. Cairns, R. C. Oldfield, J. B. Pennybacker and D. Whitteridge (229) have reported the case of a young woman who, during recurring attacks of akinetic mutism, showed disturbances of voluntary and emotional movement and an apparent loss of emotional feeling and mental awareness, coincident with distention of the walls of the third ventricle by a cystic tumour. After tension had been relieved by tapping, there was an immediate return to normal mental awareness. The study of post-traumatic disturbances by G. Jefferson (230), has led him to conclude that decreased awareness in traumatic stupor, parasomnia, may result from a focal hypothalamic or brain-stem lesion. P. Martin (231) has reported a case in which the interruption of afferent impulses to the cortex, by a small pontine haemorrhage, had resulted in somnolence, which later deepened into coma. All this evidence suggests that the changes in consciousness which are observed in catatonic stupor may be related to a disturbance of the hypothalamic driving mechanism, or to cutting off of afferent impulses from the periphery.

Failure of physical and mental adjustments to the environment is characteristic of catatonia and is shown by the absence of adequate reactions to cutaneous stimulation and the absence of avoiding reactions, such as failure to withdraw the body from an unpleasant stimulus. This non-participation is probably never volitional. It appears to be due to a lack of appreciation of sensory stimuli in their total setting, and marked inability to carry out the appropriate avoiding reactions. Painful stimuli which are not followed by adequate

responses are, however, remembered and the patient may later show that he resented the discomfort inflicted on him, although he had shown no awareness of discomfort at the time.

There is no evidence that the termination of stupor is ever subject to a patient's free choice. Sinking into stupor, on the other hand, sometimes appears to be desired, much as sleep may be desired or permitted. The diminution of mental awareness at the onset of sleep, or of catatonic stupor, must therefore be related to the volitional processes, but the means by which volition (or its suspension) can permit a change in mental awareness is still unknown. It is also unknown whether the changes involved are initiated by a physical process and whether they take place primarily at the hypothalamic or at the cortical level.

Disturbance of Eye Movements and Pupil Reactions in Catatonia.

Frequent reference is made in the literature to the "catatonic pupil"; A. Levine and P. Schilder (232) have noted inequalities in size, inconstancy in reaction and sluggishness, or complete absence of reaction to light, which they ascribed to the unbalanced action of sympathetic and parasympathetic innervation.

In the majority of early cases observed here, the pupil was widely dilated during the first days or weeks of hospitalization; dilatation could not be increased further by sensory stimulation and it was not decreased by a bright light, a circumstance which facilitated examination of the fundus. The eye movements were normal, but the patients were either unable or unwilling to fixate and therefore showed poor convergence. When an object was brought nearer to their eyes it was often examined alternately with one or other eye, or it was totally ignored; movements of convergence were quite exceptional. The absence of convergence imparts a remoteness to the features of schizophrenic patients which is portrayed in popular representations of "mad" persons. During stuporous episodes the eyes of catatonic patients were observed to rotate upwards, slightly inwards or outwards, whilst the lids were partly closed. It is noteworthy that a failure of convergence is also the most constant finding in post-encephalitic cases which show a disturbance of eye movements (W. J. Adie (233)).

Gordon Holmes (234) has pointed out that movements of the eyes are governed by the same laws as those which bring about purposive movements of the limbs, but that they are only in part voluntary or purposive. It is not merely by an effort of the will that our eyes are kept fixed on an object that interests us. Holmes instanced the case of a patient who, after recurring cerebral vascular lesions, was unable to move his eyes voluntarily. When his eyes had been fixed on a point he could follow this point while it was moved slowly in any direction, but if there was no object to interest him his eyes quickly returned to their position of rest. This case showed an inability to disengage the eyes from the object on which they were fixed, an exaggeration of the normal cortical reflex of fixation. The converse change is found in catatonic patients; like infants in the first months of life they do not fixate and they therefore fail to converge to keep an approaching object in view.

The ocular movements of a catatonic female patient, who could sometimes be aroused from stupor by an entreaty or a command, were observed on numerous occasions during the process of her arousal: there was a dissociation of eye movements before conjugate deviation was restored. The pupils remained small and the globes executed wide and independent movements in every direction, which gave the impression that they were searching space in an attempt to fuse two monocular images; one eye sometimes moved in the horizontal plane, while the other executed simultaneous vertical movements in an abducted position, with horrible cosmetic results. As stupor receded the pupils widened and the eyes resumed their normal parallel axes of movement, the immobile facial musculature relaxed and the patient regained a normal and pleasing expression. There are few references in the literature to dissociation of eye movements in adults. E. Bramwell (235) has recalled the well-known occurrence of dissociation in infants. Before fixation is acquired, the eyes of infants tend to roll in various directions and move to some extent independently. Bramwell considers that the ability to fixate determines the co-ordinated movement of the eyes, so that independent movements cease after the age of approximately 3 months. After this time the eye muscles can no longer be individually innervated and no instance could be recalled by this author in which voluntary movement of one eye, independent of that of the other, was possible, provided the ocular muscles were intact. A. Bielschowsky *et al.* (236) has, however, noted a few rare cases of disturbed fixation (in the absence of motor disorder), which are reported in the literature. He considers that this defect implies a failure of volition, possibly due to a partial dissociation (Ausschaltung) of cortical function (Rindenfunktion). Dissociated movement implies a loss of fixation, which is normally acquired by habit and practice; this loss, according to Bielschowsky, is a different matter from the loss of a performed and anatomically determined reaction.

Upward rotation of the eyes and narrowing of the pupils, when catatonic patients sink into stupor, has often been described. A Stern (237) mentions the tendency of these patients to roll their eyes upwards, and this typical catatonic feature is also portrayed in Kraepelin's work. The same ocular movements accompany the onset of sleep and are observed during mental concentration, or when efforts are made to recall a fading memory: they probably signify a folding back on the self, which is aided by exclusion of visual impressions. Stern has noted the resemblance of these upward movements of the eyes to those which occur during the oculogyric crises of post-encephalitic patients.

To summarize, the following ocular disturbances were noted in catatonic patients observed here:

- (1) A maximally dilated pupil in the early stages of the illness, with poor or absent response to light and inability, or unwillingness, to fixate and converge.
- (2) Raising of the eyeballs and constriction of the pupils with the onset of stupor.
- (3) Dissociation of eye movements during arousal from stupor, observed in one patient (a possible instance of the inability to fixate).

DISTURBANCES AT THE HIGHEST LEVEL OF THE CENTRAL NERVOUS
SYSTEM IN SCHIZOPHRENIC PATIENTS.

Any evidence which is adduced in favour of a diencephalic disturbance may also be used to point to a cortical or subcortical disturbance, if the presenting symptoms are those of dissolution. A change in the quality of mental awareness would be a convenient criterium of disturbed cortical function, if recent evidence had not suggested that this change may result from impairment at a lower level of the central nervous system. Disturbances of consciousness have been described by Jefferson (230) and by Cairns (229), following diencephalic and brainstem lesions, and deafferentiation of the cortex is reported by Martin (231) to have resulted in coma.

In these circumstances, experimental or clinical evidence of cortical dysfunction in catatonia, other than a disturbance of consciousness, must arouse special interest. Unfortunately, electroencephalographic studies have failed, up to the present, to reveal any characteristic change in patients who suffer from a functional mental illness. The records obtained during stuporous episodes of catatonic patients fail to show the well-known changes observed during normal sleep, or other states of diminished mental awareness, such as narcosis or concussion. In the words of W. Grey Walter, the E.E.G. of patients in catatonic stupor looks almost normal, although there are subtle alterations; these subtleties are usually only revealed by careful analysis and even more by what one might call "dynamic" electroencephalography, that is by providing a stimulus situation such as is known to evoke responses in normal attentive people. The absence of such responses, or their limitation to certain cerebral regions, is what seems to characterize certain psychotic states. These dynamic differences may be related to a functional isolation of cerebral areas (personal communication).

Indirect evidence that the schizophrenic disturbance may be related in some way to cortical dysfunction is drawn from the therapeutic results of prefrontal leucotomy. The nature and extent of the improvement which follows leucotomy is still a matter of opinion, but reiteration by many authorities that cases which show a high degree of mental tension are benefited most, gives a clue to the nature of the benefits which may be conferred by the operation. Even in the absence of striking mental improvement, a more philosophical (or a more passive) attitude of mind and a cheerful acceptance of remaining disabilities are not uncommon after leucotomy. Diminished mental tension may be its main socializing feature; a man or a woman with a poorly integrated personality may be less troublesome after he has learnt to "live and let live." W. Freeman and L. W. Watts (238) have reported cases in which leucotomy was followed by a disregard of severe pain due to organic illness. The operation had altered the subject's reaction to pain, without materially changing his ability to feel it, and he now described his suffering as "very bad" but added, "why worry?" This change in attitude may justify the picturesque description of the operation, given by an American psychiatrist, the "loss of the worry centre."

Suspension of voluntary movement in catatonia recalls the temporary loss

of pyramidal function, with fixation in a momentary attitude, described by Prof. G. A. Barré (239). Barré considers that this failure of pyramidal function is allied to catatonic and hysterical disturbances of motility (personal communication). A somewhat similar temporary tonic motor paralysis has been observed in non-psychotics, by G. de M. Rudolf (240); it occurred in persons who were otherwise normal and who led normal, active lives.

J. P. Murphy and E. Gellhorn (241) have produced experimental evidence to prove the dependence of cortical function on hypothalamic reinforcement; they found that simultaneous subthreshold stimulation of the hypothalamus and of the motor cortex in cats and monkeys resulted in intensification of motor discharges from the cortex. The area from which this cortical facilitation was obtained coincided with the area productive of sympathetic autonomic effects, facilitation, however, being independent of sympathetic discharges. Release from paralysis under conditions of emotional stress may also result from this form of facilitation, according to Murphy and Gellhorn. Possibly the ability of catatonic patients to perform voluntary movements when their emotions are aroused may depend on a similar mechanism.

Dissociation of eye movements in catatonic patients is further evidence of altered cortical function, the dissociation being made possible by inhibition of an acquired habitual reaction of cortical co-ordination.

Lack of perception or disregard of sensory stimuli, in the absence of organic lesions, is characteristic of catatonia and cannot be explained on the available evidence. There is also, in the catatonic, an absence of the electroencephalographic changes which denote the process of "paying attention" to incoming stimuli. The suggestion lies near that sensory stimuli may fail to arouse attention and that they may therefore remain unnoticed in consciousness, although their memory may later be revived. P. Schilder and L. Bender (242) were able to obtain both conditioned and unconditioned responses to pain in schizophrenic patients, but they found that a loss of interest and a change in mental attitude, or a possible change in the function of the brain, prevented these patients from showing any but local reactions which were dissociated from the total personality. S. Arieti (243) has commented on the insensibility of deteriorated schizophrenics, which he regarded as evidence of an agnosia, whereas Bleuler believed it to be an analgesia. Dissociation at a physical level seems the only acceptable explanation for the total disregard by schizophrenic and hysterical patients of injuries which would be expected to cause great physical suffering. A tragic example of this disregard was witnessed here in a young woman who was reputed to be suffering from the mental sequelae of encephalitis lethargica, although her history was not clear on this point, and who had shown some schizophrenic features in her thought processes. This patient was considered well enough to be discharged, but in the belief that her family did not want her she absconded. After dipping a blanket into a fire she wrapped herself in this and when found two hours later she was sitting contentedly on the floor, her legs badly burnt and her charred tibiae exposed. Third degree burns also covered her chest, abdominal wall, back and hands. She spoke pleasantly, begging to be left where she was, exculpated everybody and discussed philosophically whether the absence of religious beliefs was a

matter of importance in her present condition. This patient denied repeatedly that she was in any pain and remained cheerful and argumentative for half an hour, while her body was lifted with difficulty from the burning floorboards. She then complained of pain in her shoulders, the only part of her body which was not burnt, and a few minutes later collapsed and died.

Too little is known of the neurological and physiological processes which underlie sensory integration to attempt an interpretation of these sensory anomalies in terms of neuronal structure and function. In the case of visual perception we possess objective proof of differences in the physical backgrounds of the processes of "looking" and "seeing," which are reflected in electroencephalographic changes. When light is thrown on the eye in the form of a featureless and evenly illuminated surface, the occipital alpha activity is suppressed only when the featureless surface is scrutinized. E. D. Adrian (244) has pointed out that fixation is responsible for the suppression of occipital alpha activity. Perception of pattern, or an attempt to perceive it by discrimination and "paying attention," is presupposed in the one case and absent in the other. Non-perception of pain may perhaps depend on a similar lack of attention to incoming sensory stimuli. The patient who allowed the greater part of her body surface to be burnt, without experiencing pain, desired the physical destruction of her body in order to escape from an intolerable situation. Her attention may have been so fully engrossed in the realization of this desire that it was diverted from perception of painful stimuli. It is possible that a failure of hypothalamic reinforcement to the cortex may prevent perception of sensory stimuli, but we lack the evidence to support this hypothesis and we are still unable to explain how sensory experience can be excluded from consciousness.

PHYSIOLOGICAL CHANGES RESULTING FROM PHYSICAL TREATMENT.

Information about the physiological changes which follow physical treatment of psychotic patients is still fragmentary and the physical basis (if any) of the mental improvement initiated by these methods of treatment is still unknown. There is general recognition that improvement in the peripheral circulation and a rise in blood pressure are common during a remission. Some of the catatonic patients who were observed here suffered from vascular deficiencies and displayed features which resembled those of pituitary or adrenocortical dysfunction. Any evidence that the physical improvement noted during a remission may result from improved function of these endocrine glands would be of special interest.

E. B. Tietz and S. M. Birnbaum (245) have estimated the blood content of "adrenal hormone," a compound of epinephrine and cortical steroid (adrenalin-cortical substance A-K.), before, during and after the treatment of schizophrenic patients by insulin hypoglycaemia. They conclude from their observations that a rise in the base-line level of this compound after 4 to 6 weeks, and a raised coma value during the last weeks of treatment, are favourable prognostic signs, which usually precede a good clinical remission; these changes were present in 4 patients who recovered. Elevated levels of the hormone

during coma, unaccompanied by a raised inter-coma value, proved to be unfavourable in 13 cases, 8 of whom showed a slight improvement and early relapse. In 7 of 8 patients with low initial blood levels of this compound, in whom no rise occurred during coma, there was no clinical improvement after insulin treatment. A-K levels were high and stable after successful treatment with either insulin or E.C.T. and were low in cases of therapeutic failure.

A considerable increase in the daily excretion of 17-ketosteroids after E.C.T., cardiazol and prefrontal leucotomy, and also after testicular biopsy, was reported by R. E. Hemphill, L. D. MacLeod and M. Reiss (246). This steroid is mainly derived from the adrenal cortex and its decreased excretion follows reduced pituitary corticotrophic activity. A raised value after E.C.T., especially noticeable in cases which had a low pre-treatment excretion of 17-ketosteroid, has been attributed by these authors to raised pituitary activity. Some, but not all, chronic schizophrenics whose 17-ketosteroid excretion was raised after E.C.T. were benefited by this treatment, whereas all depressives recovered after E.C.T., whether their ketosteroid excretion was raised or remained unaltered. It is interesting to recall that H. Hoagland and G. Pincus (247) have shown that 17-ketosteroid excretion is raised after a controlled performance test, but that the rise is not commensurate with the quality of the performance. A high excretion showed a good correlation with fatigability, and with increased exposure to flying stresses.

In a recent study of the effects of electroconvulsion, W. R. Ashby (291) states that in mental patients the usual effect of convulsive therapy is a brisk outpouring of adrenal cortical steroids, during the first few days of treatment. The increase is significant in the case of the "sugar active" and "reducing" cortins, whereas excretion of 17-ketosteroids shows no significant rise in the majority of cases.

Changes in the lymphocyte count which follow exposure to stressful situations may result from increased activity of the cortex of the adrenal gland and from stimulation of a reactive adrenal cortex by adrenotrophic hormone. The changes in the lymphocyte count observed after electroconvulsion, or other forms of physical treatment, may be regarded as presumptive evidence of a rise in adrenocortical activity. A study of lymphocytic responses after electroconvulsive treatment was published by J. Carse and E. Slater (248); these observers found a systematic rise in the lymphocytic count in the 15 minutes which succeeded the convulsion, a greater increase being noted in males than in females, and in schizophrenics than in non-schizophrenics; these differences were sufficiently great to be statistically significant.

E. H. Parsons, E. F. Gildea, E. Ronzoni and S. Z. Hulbert (292) have noted that insulin coma, E.C.T. and epinephrine were followed by an immediate rise, succeeded by a fall, in the lymphocyte count of 8 schizophrenics and 6 normal controls, who submitted to one or other of these physical treatments. The 8 psychotics failed to respond to psychogenic stresses by a fall in their lymphocyte count, a finding supported by the observations of G. Pincus and F. Elmadjian (157). This failure cannot be attributed to a disorder of the pituitary-adrenal system, as the same patients responded normally to a physical stimulus, and it is therefore attributed by Parsons and his colleagues to the absence of adequate

stimulation of the endocrine glands by the central nervous system. When discussing this conclusion, G. Pincus, H. Hoagland, H. Freeman, F. Elmadjian and L. P. Romanoff (287) draw attention to the violence of an electrical stimulus, which may elicit a lymphopenic response in schizophrenic patients who have failed to respond to psychogenic stresses. The response to the specific pituitary hormone (A.C.T.H.) was defective in 4 out of 5 schizophrenics, who failed in some cases to respond to 25 mgm., but responded to 75-100 mgm. of the hormone.

After electronarcosis Linford Rees (293) has noted marked lymphocytosis during the first 5 minutes which followed treatment, and a fall below the resting level in half-hour to 2-hour readings. This fall may, in the light of our present knowledge, indicate an increase in adrenocortical activity, similar to that which follows E.C.T. and some other forms of physical stimulation.

S. Katzenelbogen, A. K. Baur and A. R. M. Coyne (249) have reported a rise in the oxygen content and the reducing substances of the blood, and a fall in carbon dioxide, after E.C.T. and metrazol convulsions. The immediate changes which result from metrazol and E.C.T. are reported by H. E. Himwich and J. F. Fazekas (250). The oxygen saturation of the blood supplying the brain is lowered sufficiently after these treatments to cause a depression of the higher centres, which is revealed by release of the lower centres. The temporary expression of more primitive cerebral mechanisms is a process comparable to Hughlings Jackson's dissolution. These authors consider that the immediate reduction of metabolic processes is important therapeutically, whereas Katzenelbogen and his colleagues point to the purely momentary deficiency of oxygen in the tonic phase of an electrically induced convulsion and believe that the secondary rise of metabolic activity is of greater therapeutic importance. L. J. Meduna (251) considers that all useful forms of shock therapy interfere with carbohydrate metabolism; the physiological effects of this interference are identical in all cases, but only a few of the patients are benefited, indicating that the response to treatment is the essential feature. This response, "phase two" of hypoglycaemic shock, as Meduna calls it, corresponds to "phase one" of other convulsive treatments; it is distinguished by a rise in blood sugar and lactic acid, an acid shift, and leucocytosis with a "shift to the left." These changes are, according to Meduna, similar in many ways to those observed during sympathetico-adrenal stimulation.

The mode of action of electrical convulsive treatment is still obscure. The possibility that a primary physiological reaction to treatment is important therapeutically is based on the slender evidence afforded by an increase in the oxygen content of the blood, and increased ketosteroid excretion after treatment. Animal experiments by L. Alexander and H. Löwenbach (252), in which currents said to be comparable to those employed in clinical treatment have been employed, offer a different explanation. They show vasoconstriction and blanching along the direct path of the current, which may last from 5 to 90 minutes. If these observations are confirmed, electroconvulsive treatment is brought into line with other modes of physical treatment, in which hypoxia and carbohydrate deprivation of cerebral tissues play a major part. Meduna adds carbon dioxide and barbiturates, as well as cyanide, to the list of curative

agents causing interference with carbohydrate metabolism; in the case of barbiturates he quotes Quastel and Wheatley (253) in support of his theory. Cushny (254) cites Damashek's view that a diminution in glucose oxidation results from the action of barbiturates. Indirect support for his theory is afforded by a study of electroencephalographic changes which follow the administration of barbiturates. The effect of these drugs is less marked and is shortened when oxygen is tendered simultaneously (J. E. Finesigen and M. A. B. Brazier (255)). Although the action of barbiturates, given in small doses to psychotic patients, is sometimes considered to increase their mental activity, improvement may be simulated by greater spontaneity in behaviour. E. Gellhorn and H. Minatoya (256) have observed that conditioned stimuli which had been inhibited at the onset, were restored after insulin hypoglycaemia. This disinhibition has been regarded as evidence of improved mental function, but it only reveals that inhibition is no longer effective. Greater spontaneity after successful physical treatment and the temporary improvement which is sometimes observed during a serious somatic illness may be due in part to this process of disinhibition. The same explanation may hold good in the case of the brief improvement in stuporous catatonics after they have inhaled carbon dioxide and oxygen. As hypoxia does not occur during carbon dioxide and oxygen inhalation, and as the cerebral circulation is improved by a rise of carbon dioxide in the cerebral blood, there may, in this case, be a real increase in the patient's ability to use higher nervous mechanisms. The benefit derived from amphetamine medication may be of the same nature, a true stimulation of the central nervous system and not merely a release phenomenon. E. Guttmann and W. Sargant (257) have noted that schizophrenic patients who suffer from a lack of initiative improve after Benzedrine treatment and display greater mental activity, whereas depressed schizophrenics are not benefited and may show a severe exacerbation of their symptoms. These results appear to corroborate the theory of a primary stimulating action of this drug, as anxiety and conflict may be more difficult to bear when mental awareness is increased.

It is difficult to regard the action of some of the physical agents for which therapeutic successes have been claimed, as being anything but "destructive." They range from strangulation (R. Rossen, H. Kabat and J. P. Anderson (258)) to hypoglycaemic coma, and a different view of their action would be contrary to physiological concepts. This view is strengthened by the evidence furnished by leucotomy. In this case, surgical isolation of a part of the cortex is frequently followed by an improvement in behaviour, a change in the prevailing mood, lessening of tension and better social adaptation. It is not yet clear whether these changes indicate the restoration of the prepsychotic personality, or a more balanced readjustment at a lower level of integration.

SCHIZOPHRENIC THOUGHT DISTURBANCE.

When discussing the nature of the mental disturbances observed in schizophrenic patients, K. Goldstein (259) has drawn attention to the inability of these patients to use abstract modes of thought, speech and behaviour. He

recognizes various degrees of complexity of abstraction, a serious impairment preventing the abstraction and isolation of mental "wholes," the selection of accidental examples, the recognition of categories and the detachment of the ego from the outer world. Goldstein discusses the results of tests commonly used to ascertain the capacity for abstract thinking (many of which were designed by himself), and concludes that the characteristic impairment of abstraction in schizophrenia is very similar to that observed in cases of organic mental illness, although it is not identical with it. The schizophrenic introduces a personal element into every test and uses projection to alter his performance under various test situations. His impairment in abstract attitude is less evident after successful treatment with various forms of shock therapy, partly because approach to the patient is made easier by this treatment. Basing his conclusions on the similarity of schizophrenic thought disturbances to those of patients suffering from an organic cerebral disease, Goldstein considers that a somatic defect cannot be excluded in schizophrenia and quotes Bleuler and Mayer-Gross in support of his contention.

I. Skottowe (260) believes the term schizophrenia as used at present to be a diagnostic label for a heterogeneous group of conditions and suggests a subdivision into three main subgroups, the dyssymbolic, dyskinetic and simple paranoid. The difficulty which is experienced by the dyssymbolic schizophrenic in formulating conceptual thought is due to his inability to use words and symbols which are necessary for more personal and conceptual thought processes. In a study of the function of language, E. L. Hutton (261) discusses the meaning attached to the words "concrete" and "abstract," as related to thought processes. These descriptive appellations possess no direct or primary sensory reference; they refer to our mode of apprehending and understanding the nature of things, our interpretations varying between these two modes of regarding. In her criticism of current tests which are used to evaluate the ability for abstract thinking, Hutton draws attention to their limitations. The ability to think categorically is not the only form of abstraction; it reflects a scientific attitude towards reality and the absence of this categorical attitude is not necessarily synonymous with reduction to a concrete mode of thought. Other forms of abstraction, which are not categorical, include aesthetic, metaphysical and religious thought. E. Hanfmann and J. Kasanin (262) have shown that in the Vigotsky test a schizophrenic tends to arrange the blocks in a physiognomic grouping and fails to distinguish between objective qualities and the emotions which they arouse. Objects with which the patients deal are not regarded by them as being either large or small but as powerful, weak, harmonious, threatening, etc., and they are used by these patients as part of their dramatic play.

J. C. Whitehorn and G. K. Zipf (263) have studied the thought disturbance revealed in schizophrenic language. N. Cameron (264) had noted that schizophrenics tended to include irrelevant elements in their test performance and that they altered the conditions and materials of their task. Whitehorn and Zipf observed a similar distortion in schizophrenic language, which they attributed to lack of concern with the social value of words, the audience being freely sacrificed to the speaker. This distortion is not a primary failure of the

processes of association, it is due to the inability of autistic persons to conform to the rules of language. The illogical features of standard speech were arbitrarily extended by these patients, new words were coined, or a different meaning was attached to existing words; Neptune became "the kind of tune Nep makes"; mother stood for "smother, nice to babies," etc. Autistic economy of mind may forbid the use of speech as a means of social communication.

Aubrey Lewis (265) considers thought disorder to be a characteristic and central feature of schizophrenia. The patient cannot command the whole range of an act of thought; he misses the point, fastens on details and brings in irrelevant associations, which are correct in themselves but divert him from the main end of his original process of thought; consequently his thinking is incoherent, rambling and jumbled. The schizophrenic brings together the most far-fetched topics; the connections are sometimes so superficial as to be empty of meaning and at another time are profoundly influenced by symbolism and highly individual values. The usual logical sequences are ignored; cause and effect are interchanged; temporal, spatial, verbal and accidental relationships are unduly turned from abstract to concrete, treated as grounds of identity, played with or flouted. Things linked only by analogy and chance association are taken to be the same. The condensation of several conceptions in one, or transference of a set of attributes to some inappropriate object, may become a matter of course, so that only the closest knowledge of the patient and his surroundings will enable the psychiatrist to follow his meaning. It is not necessary, however, that such extreme incoherence be evident in the patient's talk; he may not show any at all when speaking, or he may suddenly obtrude a startling lapse from normal ways of thought, which he then ignores, justifies or explains away. Inconsistent thoughts can be present together, in a way impossible for normal people; and the same object or notion can appear to him in several interchangeable guises, each of which would normally exclude the others. The patient himself is often aware of his disordered thinking and may describe it; he feels his thoughts are suddenly taken out of his head, other thoughts foreign to him are put into his head, his mind is not his own, his thinking is suddenly interrupted, some external power controls it.

An indirect approach to the study of schizophrenic thought disorder is offered by observation of changes which follow leucotomy. In patients who have shown characteristic blocking of thought, the subsidence of emotional tension after leucotomy may relieve this disability and may sometimes restore almost normal speech, although schizophrenic features may persist in the content of thought. The difficulty which is experienced by normal persons in finding words when they are overwhelmed by joy, sorrow or anger, and the disruption of normal thinking and behaviour by overwhelming emotion suggest that improvement in schizophrenic speech, and greater freedom in schizophrenic thought after leucotomy, may be related to lowering of emotional tension. When discussing the effects of this operation, W. Freeman and J. W. Watts (266) have concluded that the ideational processes which are generated in the frontal lobes are not disturbed by lobotomy; lack of emotional charge may permit a patient to direct his thoughts outwards after a successful lobotomy.

It is surprising that in discussions on schizophrenic dissociation reference is seldom made to "thought-splitting" occurring in normal persons. Catathymic thought may emerge into consciousness and may coexist for a time with a simultaneous stream of "normal" thought; the two processes may then be so intimately mixed that their sequence or actual concurrence is difficult to determine. The emergence of catathymic thought is obviously related to day-dreaming, but reasoned processes need not be seriously disrupted, and introspection may reveal that autistic components have coexisted in consciousness when the attention seemed to be fully engaged on an absorbing occupation. The less rational components of thought may only be revealed by a sudden realization of the oddity of one of their features, an image, for instance, which is grotesque in itself or in contrast with its surroundings. When the immediate antecedents of these mental events are recaptured, they are found to belong to thought processes which are sometimes described as "primitive" and which are more familiar in dreams. They are rich in elusive imagery, apparently inconsequent and incongruous, but not necessarily devoid of reasoned elements of thought. A deduction drawn from a logical process of reasoning may cause surprise when the premises on which it is based are not perceived in consciousness. More commonly only the affective colouring of these mental events is experienced, for instance, the awareness of ungrounded pleasure or anxiety. Autistic components of conscious thought are more conspicuous and less scattered after the onset of mental and bodily fatigue and they may then be very similar to the thought processes of schizophrenic patients. In persons who are not given to self-analysis these autistic components remain unnoticed unless dreams or day-dreams are recalled, but their importance in shaping experience becomes apparent when individual differences in appreciating new experience are considered. These differences have been illustrated by F. C. Bartlett's striking experiments (267). New experience is an individual event which is shaped by every aspect of a person's past and present mental and physical activity, and by experience which is, and that which is not available in consciousness. In the schizophrenic the "rational components" of thought are tolerant of their catathymic partners; these are neither discounted nor accorded different treatment, and the two processes of thought may run in double harness. A schizophrenic may, however, be aware that other modes of thought are available to him and that a firmer contact with reality can be established; this awareness and his refusal to establish such contacts have been frequently recorded, often by the patient himself. He may express in words his refusal to face new experience in a way his past experience has taught him to avoid, as it involves greater mental suffering: "It hurts too much," "I can't," etc.

Characteristic "clearness" is sometimes said to distinguish schizophrenic hallucinatory experience, but clearness is limited to the absence of gross changes of consciousness, such as are present in patients suffering from delirious or stuporous states, and in normal persons who are asleep. This "clearness" does not imply that the hallucinatory event is experienced by a person who is enjoying the full use of relatively normal and rational processes of thought; the credence accorded to the hallucinatory event is proof that the patient's

judgment differs in quality, or degree, from that of a normal adult. If we adopt the definition of a conscious process given by T. Tennent (268), this process implies awareness of ourselves and our surroundings and involves the ability to synthesize and integrate as well as evaluate new experience. The thought processes of the schizophrenic who lacks the ability to synthesize and integrate and fails to evaluate his experience, cannot be regarded as fully conscious, in the light of this definition.

In a discussion on the early diagnosis of schizophrenia, W. Mayer-Gross (269) has referred to changes in volition of which the schizophrenic is sometimes aware. He may not feel master of his will, or of his thoughts and activities, and may conclude that he is influenced or drugged by others. C. G. Jung (270) follows Janet in accepting the occasional occurrence in normal persons of an "*abaissement du niveau mental*," during which the train of thought cannot be pursued to its logical end. In a neurotic individual an eruption of "the unconscious" may produce a temporary "*abaissement*," but in the schizophrenic the eruption may be sufficiently violent to disrupt the central control of the whole personality. The ensuing disintegration has been regarded by Bleuler as evidence of the destruction of the processes of association. Pre-existing weakness of the will may predispose to these violent changes, or they may be a result of the force of the eruption. Jung finds it difficult to explain how an "*abaissement*," which is sufficiently violent to destroy the unity of the personality, can be initiated by a psychological event, but his experience has led him to believe that the majority of schizophrenic illnesses are determined by psychogenic causes.

INTELLECTUAL DETERIORATION IN CHRONIC SCHIZOPHRENIA.

E. Bleuler (3) believed that mental deterioration was more apparent than real in dementia praecox. A similar view is expressed by Sir David Henderson (271) and by Prof. Aubrey Lewis (265) and is tacitly adopted whenever a good remission is claimed for a case of chronic schizophrenia. The loss of mental faculties could not have been irremediable if they were later restored to the patient.

C. Macfie Campbell (272) considers that true mental deterioration occurs only in patients who suffer from a constitutional inadequacy and show no special trends in an insidious schizophrenic illness. He was unable to find a physical cause for this mental deterioration and attributed its occurrence to the parasitic personality of these patients, their low vitality and abiotrophic inadequacy.

Many of the hebephrenic cases which were observed at this hospital conformed to Campbell's clinical description. In the later stages of their illness they were indistinguishable from cases of mental deficiency and appeared to be suffering from true mental deterioration. However, in a few cases which were clinically indistinguishable from the others, an astonishing return, or unveiling, of higher mental activity was witnessed. It may be wiser to consider that a schizophrenic illness never involves the irremediable loss of higher mental faculties.

In his report on the favourable results of psychoanalytic treatment of deteriorated schizophrenics, J. N. Rosen (273) has noted the absence, in these

patients, of irreversible organic or constitutional changes and the absence of intellectual deterioration. P. Hoch (274) believes that the improvement noted by Rosen after psychoanalytic treatment is the result of lessened emotional tension, a feature shared by all successful methods of therapy, but he agrees with Rosen that "deterioration" in schizophrenia is frequently only a sign of mental regression and that under favourable circumstances it can be temporarily reversed. G. Ernst (275) has described her psychotherapeutic approach to deteriorated schizophrenic patients who had been in hospital for 20 years. These patients were not demented, as some of them were aware of their predicament, but all were disinclined to return to a state of increased mental awareness. When they were urged to resume a firmer contact with reality they gave such answers as "I cannot," or "I shall lose too much," etc. Ernst was able to converse with them by means of drawings and by posturing, and noted their difficulties in verbal expression. They appeared to be suffering from the dyssymbolic failure which was described by Skottowe.

Deteriorated patients who were observed here differed in some respects from those described by Rosen and Ernst. They were frequently difficult to approach, but when their mental resistance was overcome they showed no special difficulty in verbal expression. A female "dement," for instance, who had spent many years of her life engaged in crossing and recrossing a ward, while emitting a bellowing sound, answered the question, "Are you Swiss?" which was suggested by this imitation of the noise of cattle, by an instantaneous "Canton Appenzell." These were the first words spoken by her for years. Similarly, an afternoon spent in a padded room with an unruly, seemingly demented and mute schizophrenic, who walked on all fours, continually knocking her head against a wall, ended in free conversation. She was aggressive when exhorted repeatedly to "stop all this silliness," but after the contest had continued for some hours she suddenly said, "Jealousy is an awful thing." A few minutes later she was prevailed upon to tell a coherent story, which she introduced by saying, "It is a terrible thing to starve a child." This is what she had done, or thought she had done, in order to retain her husband's love. These were not isolated cases and at least 3 other mute or incoherent schizophrenic women and 4 men were engaged in free conversation when their defences had been penetrated after some hours of intense effort. No good therapeutic results followed this enforced return to free social intercourse. Every patient objected to the prolonged interview and all showed their displeasure by unmistakable signs of growing animosity which amounted in some cases to scarcely veiled threats of physical violence. These circumstances discouraged the further use of this method of investigation.

Apparent deterioration in chronic psychotics who have spent half a lifetime in hospital is sometimes a result of their habituation to faulty reactions and conditioning in the Pavlovian sense. The work of E. Gellhorn (256) has shown that disinhibition occurs in experimental animals after electroconvulsion. If his observations receive clinical confirmation they may help to explain the ease with which schizophrenic patients can be approached after various forms of physical treatment. The loss of recently acquired inhibitions may assist in establishing more favourable reactions to their environment.

NOSOLOGICAL ENTITY AND UNITY OF SCHIZOPHRENIC ILLNESS.

No definition of schizophrenia has received general assent, although the definitions proposed by various authorities have much in common. Agreement does not, however, extend to a subdivision of the illness into separate syndromes. When discussing the difficulties of psychiatric diagnosis, J. H. Masserman and H. T. Carmichael (276) have pointed out the stability of a primary diagnosis of schizophrenia compared to the unreliability of its subclassifications. While the primary diagnosis is seldom reversed, follow-up studies have proved that shifting of patients from one subcategory to another is almost the rule. There is also much uncertainty as to which syndromes should be included under the heading of schizophrenia. If an abnormality of behaviour and marked personality changes are considered necessary for inclusion under this heading, a circumscribed paranoid reaction would probably not be included. If true mental deterioration is not considered to occur in schizophrenia, some cases of hebephrenic illness would have to be described as instances of an abiotrophic process. More or less theoretical limitations may exclude schizophrenic reactions to organic illness and, at the opposite end of the scale, the purely reactive schizophrenic syndromes, but each time the inclusion or exclusion of a syndrome under this heading is debated, this doubt is evidence of its similarity to schizophrenia.

Bleuler regarded loosening of the normal processes of association as the fundamental feature of a schizophrenic illness and believed that an organic cause was one of the cardinal factors responsible for the illness.

Aubrey Lewis (277) defined schizophrenia, for diagnostic and clinical purposes, as a form of maladaptation in which there are characteristic defects of inner harmony and consistency in behaviour, thought and emotion. Although the illnesses included under this name are diverse, detachment from the world without and breaking up of normal psychological connections within is common to them all.

R. G. Hoskins (122) regards schizophrenia as a defect of adaptive efficiency which occurs in patients who show faulty instinctive and acquired reactions. In Hoskins' opinion schizophrenic autism arises from suppressed awareness as an escape from affective harassment, the schizophrenic syndrome being best described, in Kraepelin's words, as the ensuing "disorganization of the inward coherence of the psychic personality."

H. D. Singer (278) has attributed psychotic illness to a primary structural lesion of the central mechanism of autonomic integration. In Singer's view the psychosis reveals a patient's power of adaptation to whatever the causal lesion has left intact, and individual differences in autonomic and metabolic constitution determine the forcefulness of active readjustment.

In these and other definitions of schizophrenia the malady presents two salient features, loosening of internal ties and detachment from the world without. The order in which these changes are considered to arise depends, in part, on the acceptance or rejection of a causal organic factor. The possibility that schizophrenic reactions are dependent on organic changes is not generally accepted but is mentioned by several authorities, Bleuler (3), Singer (278),

Goldstein (259), Mayer-Gross (279), etc. No proof of causative organic changes is yet available, with the exception of evidence in favour of genetic predisposition. F. J. Kallman (280) has presented statistical evidence of a higher morbidity rate in monozygotic co-twins than in dizygotes and siblings, an indication, in his opinion, of a constitutional inability to resist the progression of a schizophrenic psychosis. E. T. O. Slater (281) has concluded from his statistical study of schizophrenic siblings that a particular symptom is related to the time of onset of the psychosis, the patient's body-build and the remitting, chronic or dementing course of the illness. Paranoid features were found more frequently in patients of pyknic build, whereas catatonic features predominated in those of asthenic habitus. The importance of a constitutional and therefore of an organic predisposing factor in schizophrenia appears to have been established by these genetic studies.

Constitutional endowment includes vascular, endocrine and autonomic functions, their maturation and interplay during development. More subtle distinctions between individuals in which psychological factors play a more prominent part, a "good" or "poor" personality, good and less satisfactory integration, etc., may also prove to be determined by constitutional endowment. This possibility does not compel belief in an organic predetermination of human behaviour, as it remains true that a poorly endowed person may overcome most of his disabilities by sufficient exertion and adequate motivation, but as the load increases the possibility of a breakdown must become greater.

There is no general agreement on the importance which should be attributed to the physical manifestations of schizophrenia. F. Alexander (282) has drawn attention to the difference between physical signs which are physiological by-products of a mental disturbance, such as the autonomic manifestations of fear, and those which offer relief from psychological distress by their symbolic value as, for instance, hysterical conversion. The physical signs observed in catatonia do not readily fall under either of these headings; they are probably "adaptive phenomena" which favour the development of a catatonic reaction. Secondary physiological changes, such as peripheral vasoconstriction, are evidence of adjustment to altered physiological conditions. These physical changes are, as a rule, absent in schizophrenics who suffer from a paranoid syndrome and they are therefore not essential to the development of at least one form of the psychosis.

Transient catatonic and paranoid reactions are not uncommon in organic disorders. Catatonic states may develop in the course of almost any organic cerebral condition. Paranoid reactions, in post-encephalitic patients, have been described by M. Critchley (283) and paranoid misinterpretations, which tended to become systematized, were noted in dysergastic reactions of toxic, infective and metabolic disorders by H. G. Wolff and D. Curran (284). To these organically determined paranoid reactions one may perhaps add the persecutory delusions experienced by senile patients. The aetiology of so-called organic schizophrenic reactions remains obscure. There is no proof that an organic lesion can initiate the complex changes which lead to a schizophrenic illness, and predisposition to the psychosis cannot be excluded in the majority of cases. K. Goldstein (285) has described a "catastrophic reaction" in patients

who suffer from the after-effects of severe head injury when they are faced with a difficult task. Earlier observations by H. G. Wolff and D. Curran (284) have shown that patients who suffer from delirium or from an allied mental disturbance find sustained mental effort more difficult and become more suspicious and more hallucinated in circumstances which demand greater discrimination. K. Goldstein noted similar reactions in schizophrenic patients and is inclined to attribute them to an organic factor responsible for the schizophrenic syndrome.

The small number of "schizophrenic" patients in whom true mental deterioration has occurred may be suffering from an abiotrophic process, but there is no evidence of any structural change in the brain of these cases. The absence of histological changes in the brain of some of the patients who suffer from congenital mental defect reminds us, however, that our methods of investigation are still inadequate and that better methods may support a conclusion which is at present based on clinical observation.

In conclusion, reference should be made to the phylogenetic aspect of schizophrenic illness. The extensive biological investigation of J. G. Byrne (286) into the behaviour of various animals exposed to conditions of environmental stress has led him to formulate general conclusions which are applicable to the interpretation of human behaviour and its psychotic aberrations. He has noted that a choice of three reactions is available to most organisms in response to external stresses, and that they may choose an "avoidance," a "still or static," or an "approach" reaction. It is evident that the schizophrenic prefers the first or second of these alternatives, whereas a normal person may choose (within individual limits) whichever response appears to him to be most appropriate to the occasion. A "still reaction" has a wide range of biological usefulness and can assume different guises according to the functional level at which it is evoked. At the lowest physiological level the still reaction is manifested by feigning death, at an intermediate level by muscular tension, and at a higher psychological level by immobility of emotional expression. The same idea underlies the differentiation of behaviour into "*ab und zu Reaktionen*," adopted by German psychologists. Darwin's work on the expression of emotion is also helpful in explaining the psychosomatic disturbances of mental patients. The heritage of human expression indicates a purpose which has become less evident, but which is still revealed by a fixed neurological pattern, for instance, the tension of muscles when immobilization is imperative, or complete flaccidity when fear counsels surrender. The work of the biologist and experimental psychologist helps to explain the "purpose" of some of the common catatonic reactions, particularly of catatonic stupor. Stupor severs the link with reality and temporarily protects the individual from contact with hurtful or threatening surroundings.

SOMATIC MANIFESTATIONS OF SCHIZOPHRENIA IN THE LIGHT OF THE PRESENT STUDY.

Personal observation shrinks into insignificance compared to the volume of recorded evidence, but it serves as a guide to the work of others when this is incomplete or contradictory. The literature of schizophrenia is possibly more extensive than that of any other disease. The study of its clinical forms

has been the concern of the psychiatrist, its incidence and causation have been investigated in the light of the more recent sciences of statistics and genetics, but the interpretation of the illness in the general framework of human behaviour has aroused less interest.

The present study of the somatic manifestations of schizophrenia has shown the dependence of the vascular disturbance on compensatory vasoconstrictor reactions. The body temperature is sufficiently maintained by this means to assure survival, although the peripheral structures may be injured by excessive reduction of their blood supply. When the external temperature is lowered, the surface temperature of a schizophrenic falls to a lower level than that of other psychotics exposed to the same environmental conditions; the schizophrenic fails to respond to increased demands made on him by altered external circumstances. Vasoconstriction of the main limb vessels and of the retinal arteries in catatonic patients suggests that confusion and asthenia may sometimes be secondary to the vascular deficiency when these two conditions coexist. As the average blood pressure of refractory (mainly catatonic) schizophrenics was found to be lower than that of paranoid and socialized patients, and as improvement in the systemic circulation coincided with the onset of a remission, it is possible that some of the abnormalities of behaviour observed in refractory patients may be related to a relatively inadequate cerebral circulation.

Evidence of minor and reversible endocrine disturbances were present in many of the schizophrenics examined. Cutaneous changes, resembling those seen in thyroid deficiency, or the occurrence of asthenic states, suggested a pituitary or adrenocortical dysfunction, while changes in the appearance of the vaginal mucosa and prolonged periods of amenorrhoea gave evidence of diminished ovarian function. Metabolic unresponsiveness, attacks of ketonuria and minor changes in sugar tolerance point to a disturbance of metabolic function. The physiological disturbance of the central nervous system extends to its highest level; changes in mental awareness during stupor, altered reactions to painful stimuli and dissociation of conjugate eye movements in catatonic patients indicate a disturbance of cortical function.

It is generally agreed that the clinical syndromes of schizophrenic illness share a common feature, a loss of unification of the personality, which is termed "dissociation." This disintegration of the personality, usually regarded as a primary factor of schizophrenic illness, has led to the adoption of a generic name for a number of syndromes which have little else in common. It is possible, however, to view the cleavage of the personality as a secondary event, the result of an adaptation to relatively excessive demands made on a predisposed person. If this view is adopted, severance from the "environment," the word being used in its broadest sense, may include rejection of that part of the personality which is concerned with recognition and evaluation of empirical experience. The schizophrenic rejection may assume one of two forms, which are not mutually exclusive, paranoid projection or grosser catatonic withdrawal. Catatonic withdrawal, and possibly all schizophrenic reactions show a somatic as well as a mental aspect. In the case of catatonia the physical changes are those which facilitate, and under some conditions possibly initiate,

schizophrenic non-participation. Lowering of the metabolic level, vascular deficiency, reduction in endocrine function and local instead of general responses are examples of this somatic detachment. Paranoid reactions are more circumscribed and more limited to the mental level, but what is known of the physical changes which underlie mental processes, particularly the process of paying attention, suggests that in both forms of the psychosis withdrawal is assisted by the isolation of physical functions necessary to cognitive appraisal. In catatonia cognitive disregard is more complete, while in paranoid schizophrenia it is limited to one or more delusional systems. Unacceptable emotional content may suppress hypothalamic reinforcement, which may be necessary for adequate cortical function, but this is still a purely hypothetical supposition.

Although catatonic and paranoid reactions are in many ways complementary, and may occur in the same patient concurrently, or in succession, they are more frequently separate. Evidence has been adduced that their incidence is genetically determined and that their occurrence is related to the type of body build and therefore to the size of the organs, the function of the autonomic system, vascularity, endocrine balance, etc. It seems possible that differences in constitutional endowment may account for the clinical varieties of the psychosis, while the common feature in different forms of schizophrenic illness should be sought in a characteristic diminution of the quality of critical appraisal. Impairment of this quality does not result from a loss of intelligence, the capacity for appraisal being temporarily set aside by an intelligent schizophrenic in a manner which is not adopted even by a stupid non-psychotic. The wealth and intensity of autistic experience in schizophrenia hinders abstract thought and prevents the appraisal of objective reality; it may be responsible for misinterpretation, distortion and delusions, and for the resulting changes in reality feeling. The difficulty which is experienced by the schizophrenic in directing his thoughts must depend in part on his ability to direct autistic components springing from motives and impulses not accessible to volitional direction. There is no reason to suppose that the schizophrenic voluntarily rejects ordinary modes of thought, but there are indications that he is often aware of his detachment from reality and that he jealously guards this knowledge; all that remains to him of security is threatened by enquiries into his motives or by attempts to correct his misinterpretations. His acquiescence in the schizophrenic solution is perhaps inversely proportional to the weight of predisposing factors, and in so-called organic schizophrenic reactions the element of consent may be non-existent.

These considerations have a bearing on the treatment of schizophrenic patients. Their severance from reality is never complete and the possibility that a schizophrenic may be induced to adopt more normal reactions and a firmer contact with reality remains almost to the end. Spontaneous remissions after the failure of physical and psychological treatment are not unknown and show our present therapeutic helplessness and the need for a better understanding of the nature of this improvement. Recognition of the frequent coincidence of physical improvement, particularly of the vascular deficiency, with the onset of mental remission should encourage the use of therapeutic

measures directed towards the correction of these physical abnormalities, in the hope of assisting mental recovery.

The schizophrenic retreat from reality is a faulty but purposive adaptation, in which somatic and mental components concur. This interpretation of the physical signs of schizophrenia co-ordinates some of the aspects of our rapidly increasing knowledge. The present study was undertaken without intent to prove any particular theory, but as clinical experimentation and observation proceeded, and as the literature was more extensively consulted, the total evidence appeared to be directed towards the same conclusion. The consensus of published opinion was not contradictory to the views expressed in this study and frequently gave them direct support.

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EXPERIMENTAL STUDIES ON FRONTAL LOBE FUNCTIONS IN MONKEYS IN RELATION TO LEUCOTOMY.*

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INTRODUCTION.

PREFRONTAL leucotomy as an operative method of treatment for mental disease greatly stimulated research into the functions of the frontal lobes. The operation was a direct result of the observation of Fulton and Jacobsen (1935) that rage reactions seen in monkeys in the course of increasingly difficult experimental tasks do not occur after extirpation of the frontal lobes.

Most investigations on behavioural changes in animals are based on material where the whole prefrontal cortex was extirpated. Fulton (1943) states that after such extirpation monkeys and chimpanzees are more restless and distractible, exhibit a fatuous equanimity of spirit, their capacity for recall is impaired and their reactions are largely influenced by immediate sensory experiences. The animals are described as "living in a perpetual present." Bard and Mountcastle (1948) were able to produce a state of apathy in cats by bilateral removal of the frontal areas. They point out that for the production of this state it is necessary to spare certain areas of the orbital cortex and rhinencephalic structures near this region. Similar changes are not found after removal of other cortical areas, Jacobsen and Elder (1936).

Our knowledge of the functions of the different areas of the prefrontal cortex is still incomplete. Ruch and Shenkin (1943) showed that the hypermotility previously reported after bilateral frontal lobectomy occurs only when area 13 is injured. Richter and Hines (1938) and Mettler (1945) believe, however, that hyperactivity occurs only when the prefrontal cortex lesions are combined with damage to the striatum. Meyer and McLardy (1948) found that cases with striatal and without orbital damage showed the same incidence of restlessness. Fulton, Livingston and Davies (1947) indicate that fibres projecting to area 13 pass through the caudate nucleus, which might explain this phenomenon.

Prefrontal leucotomy, as carried out in man, is a blind operation and the lesions, therefore, can be much less precisely located than in previous experimental studies. Most techniques, such as that of Freeman and Watts (1942),

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lead to extensive separation of the prefrontal cortex from lower structures. More limited lesions were suggested by Dax and Radley Smith (1943) and others. Their experience taught them to avoid lower and posterior cuts in very excited and restless patients. The first object of the present investigation was an attempt to show any possible correlation between the type of cut and the resulting behavioural changes.

The present state of our knowledge of the anatomy of the prefrontal cortex and its connections was recently reviewed by Le Gros Clark (1948). He states that the prefrontal lobes should be regarded, not as association areas, but primarily as afferent projection areas. Le Gros Clark and Boggon (1933) had already observed after experimental studies that a large part of the frontal lobe is a projection area for the dorsomedial nucleus (D.M.N.) of the thalamus. Meyer and McLardy (1947) and Freeman and Watts (1947) showed that the areas of the prefrontal cortex are connected with certain sub-divisions of the D.M.N. in the thalamus. The central part of the D.M.N. was found to be connected with the frontal pole, the lateral portion with the convexity, and the medial portion with the orbital surface.

The second object of our investigations was to discover whether the same behavioural changes result from lesions of the D.M.N. as result from lesions of the prefrontal lobe.

MATERIAL AND METHODS.

Monkeys of the Rhesus macaque type were used for all experiments. Anaesthesia was carried out with Nembutal 0.6 mg. per kilo body weight. A large exposure was always performed by a frontal osteoplastic flap. After removal of the dura, the motor area was located by electrical stimulation in each case.

The leucotomies were performed with a blunt leucotome penetrating the cortex at the posterior and lower end of the sulcus rectus in front of the sulcus arcuatus, that is to say, at the rostral border of area 8. There were three types of subcortical leucotomy:—

1. A complete leucotomy in the coronal plane to a depth of 1.5 to 2 cm., covering the whole area of the frontal lobe. (See Fig. 1) (M.Th.L. 9, 13.)
2. A leucotomy in the horizontal plane. (See Fig. 2) (M.Th.L. 11.)
3. A leucotomy of only the lower orbital part in the coronal plane. (See Fig. 3) (M.Th.L. 12.)
4. A leucotomy in the coronal plane further posterior (M.D.M.2).
5. For attempted lesions of the thalamus, the Souttar-Beattie stereotaxic instrument was employed (M.D.M.1, M.D.M. 3, 4). The instrument consists of a suitable length of hypodermic needle tubing of diameter $1\frac{1}{2}$ mm. in which is concealed a spring-loaded steel knife. When the needle has been inserted to the required depth the spring-loaded steel knife is pushed out and the centre point of the knife can be moved laterally. In the present experiments the knife was pushed in at right-angles to the Rolandic fissure to a total depth of 2.5 cm.; when right in the knife was rotated. The cortex was gently withdrawn from the midline to allow insertion of the knife about 2 mm. from the midline. This was repeated on the other side. (Glees, Wall and Bright, 1947.)

6. A bilateral thalamic lesion by surgical exposure of the thalamus.

M.Th.L.10.—In this monkey an attempt was made to make an extensive lesion of the medial region of the thalamus by direct exposure. The corpus callosum was opened and the motor area identified by electrical stimulation. Finally, the medial portions of the thalamus were destroyed by suction.

The animal unfortunately died after 24 hours without recovering consciousness.

This was the only attempt to cause a thalamic lesion by visual control. The difficulties of this extensive surgical approach are too great to follow up the effects of chronic lesions necessary for this study.

The neuro-histological investigation of the brains was carried out by using the Marchi technique (Swank-Davenport modification), the Nissl stain for retrograde cell changes, and the Heidenhain technique for normal myelinated nerve fibres. The Marchi (Swank-Davenport modification) proved of great use, not only for following degenerating fibre tracts, but also for observing retrograde cell changes. (Glees, 1947).

In each animal behavioural changes were recorded and special psychological tests were given to some animals. Delayed reaction tests were made on the four monkeys: M.Th.L.13, M.D.M.1 and M.D.M.2; in M.D.M.3 tests were started only after the operation, while in the other three cases a measure of "immediate memory span" was made before and after the operation. The test consisted simply in placing food under one of three identical mugs within view of the subject, lowering a screen for varying periods of time, then noting which mug the monkey lifted when the screen was raised. In working out the results, a correction was made for chance right solutions, then a "limen of immediate memory" calculated, representing the period of time after which 50 per cent. correct responses would be made. The value varied from day to day for individual monkeys, also; immediate-memory span appeared to be twice as good when the bait was ripe pear instead of apple. These tests could, unfortunately, not be given to every operated animal and only tentative conclusions can therefore be drawn.

RESULTS.

Complete Bilateral Leucotomy in Coronal Plane. M.Th.L.9 (Fig. 1).

(a) *Behavioural Changes.*—For the first experiment a very aggressive female monkey was used. She had to be separated from the others because of continual fighting.

On the day following the operation, her behaviour was markedly changed; the animal was very quiet and inactive, allowed herself to be touched, and took sugar from the observer's hand; there was some piloerection along the trunk. Eye movements were preserved. The animal continued to be indifferent and inactive on the following day. She made frequent circling movements in both directions; the left hand was not used at all and appeared definitely weaker. Eight days later she was still apathetic. When the cage was tapped the animal turned her head slowly and showed no fear reaction. She was taken out on lead and made no attempt to escape. Ten days after the operation the monkey

was still very apathetic, although on one occasion she chased a cat. As time went on the animal gradually became more active, and reacted more to her environment, but continued to show much less fear than before the leucotomy. The animal was killed 77 days after the operation.

(b) *Neuro-histological Findings*.—Although a complete leucotomy was attempted, it was found from sections in a more posterior plane that the orbital surfaces were less involved than had been expected.

A considerable loss of cells was found on both sides in the dorso-medial nucleus of the thalamus. However, the degeneration of cells in the thalamus was limited mainly to the lateral portion of the D.M.N. (c.f. M.Th.11). As the injury of the dorsal portions of the frontal lobes had extended back into the motor area, through post-operative necrosis, both pyramidal tracts showed Marchi degeneration in the spinal cord, more concentrated on the left than on the right. The involvement of the motor area explains the slight degeneration which is observable in the nucleus ventralis lateralis.

Complete Bilateral Leucotomy in Coronal Plane. M.Th.L13 (Fig. 1).

(a) *Behavioural Changes*.—Before the operation this monkey was very nervous; when stared at he would make exaggerated ear, scalp and lip movements, with continued mouth gaping, and jerky movements of the whole body about once a second; this pattern of behaviour might last several minutes before gradually disappearing. It was a highly exaggerated form of the startle reaction seen in most rhesus monkeys. Twelve days before the operation the monkey escaped, and subsequently developed a "neurotic" tendency to avoid the front of the cage. If offered food from the front, his behaviour appeared typical of an approach-avoidance conflict, resulting in vacillation.

Immediately after the operation the animal was slow (but with no obvious motor impairments), tame and gentle. There were no jerky mouth, eye or body movements. On the whole the animal showed eagerness when being experimented on, but there were sudden losses of interest, of increasing frequency. After four weeks the animal was gentle and unexcited, but occasionally made sudden "irritable" snatches at the experimental apparatus. At this time, walking in circles (mostly clockwise), which had been seen frequently just after the operation, was seen only occasionally.

After five weeks there was a sudden increase in excitability and activity, including a backward and forward dash every two seconds. After six weeks, just before the animal was killed, excitability and fear reactions were nearly back to the pre-operative level, with occasional mouth-gaping, but without the specific jerky movements. The "phobic" attitude to the front of the cage did not return.

At three weeks after the operation there had been a measurable "immediate memory span," but this was lost after a week, largely through the tendency to perseverate on one response. (See Discussion.)

(b) *Neuro-histological Findings*.—The lesion involved, on the left side: the corpus callosum, caudate nucleus, anterior limb of internal capsule and putamen; on the right side the damage to the corpus striatum was only slight. The lesion reached the orbital cortex. The dorso-medial nucleus of the thalamus

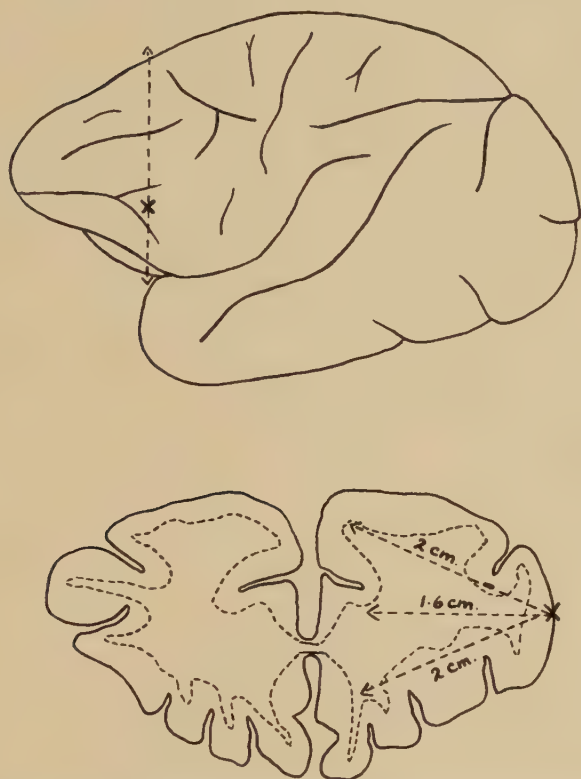


FIG. 1.—A diagrammatic representation of the plane of leucotomy and depth of incision in the monkeys M.Th.L.9 and 13.

in both sides showed gross signs of nerve cell degeneration in its medial and lateral parts and the beginnings of proliferation of glia cells. Cell changes were found also in the N. ventralis anterior and in the antero-medial nucleus.

Leucotomy in the Horizontal Plane. M.Th.L.11 (Fig. 2).

(a) *Behavioural Changes.*—A rather apprehensive female animal was selected for operation. On the day following the operation the animal was hyperactive, and restless, walking up and down the cage. When it passed the gate it grasped it and jumped up and down. The behaviour seemed somewhat stereotyped; the animal over-reacted to external stimuli. Three days after the operation the animal continued to show this hyperactivity together with piloerection.

After about 16 days the hyperactivity had more or less subsided and the monkey continued to be much quieter until it had to be killed 68 days after the operation, because an oedema had developed from the waist downwards. Post mortem examination showed a severe interstitial hepatitis with destruction of the liver parenchyma.

(b) *Neuro-histological Findings.*—The sections of the frontal lobes showed that it was mainly the fibres to and from the dorsal aspects of the frontal cortex which had been severed, while the connections of the orbital cortex were not interrupted. Sections of the thalamus stained with the Nissl method

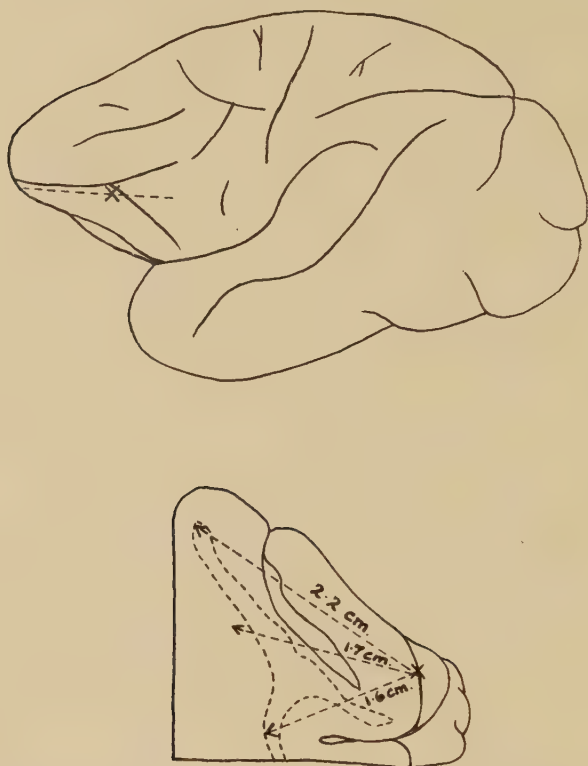


FIG. 2.—Plane of leucotomy and depth of incision in M.Th.L. 11.

revealed that the lateral portions of the D.M.N. had undergone retrograde changes.

Bilateral Leucotomy. M.Th.L.12. (Fig. 3.) Lesion of the lower orbital part in the coronal plane.

(a) *Behavioural Changes.*—A male monkey was used for this operation. On the day following the operation the animal appeared lively and alert. It showed some hyperactivity with continuous circling movements clockwise and anti-clockwise. This became even more marked three days later. The hyperactivity with circling remained present throughout the period of observation; it did, however, gradually become less marked. The animal always remained fearful and alert, and was killed 83 days after the operation.

(b) *Neuro-histological Findings.*—The degeneration of fibres and cells in the Marchi preparations was very well marked in this monkey and retrograde degeneration could be clearly followed.

Sections of the frontal lobe showed that the lesion involved the orbital part of the frontal lobes, and also the genu and anterior limb of the internal capsule, so that fibres other than those coming from the frontal lobe were intercepted; damage to the anterior portions of the striatum on the left side was observed.

The fibres from the frontal lobe enter the D.M. nucleus by passing through

the thalamus, leaving the internal capsule at the level of the genu to enter the thalamus.

Marchi material of the thalamus showed degenerating cells in the anterior portion of the dorso-medial nucleus, the pars magnocellularis or medial part being most heavily affected. (These cells show up because of the fatty



FIG. 3.—Plane of leucotomy and depth of incision in M.Th.L. 12.

degeneration which is Marchi positive.) As the internal capsule was damaged, degeneration in various other fields was seen, namely in the middle peduncle, the A.V. nucleus of the thalamus and in Forel's field. Fibres were also seen tracking towards the centre median nucleus of the thalamus on the right side.

Posterior Leucotomy in the Coronal Plane. M.D.M.2.

A bilateral lesion of the medial nuclei of the thalamus was attempted but histological examination showed that the lesions were mainly anterior to the thalamus and because of this the case is grouped under bilateral leucotomy, the type of injury being similar to a very posterior leucotomy.

(a) *Behavioural Changes.*—Before the operation this female rhesus was very tame, gentle and co-operative, compared with the majority of the monkeys reported here, none of whom were given time to become acclimatised to rigorous experimental treatment. She was not easily distractible, but occasionally lost interest.

After the operation, for the first five weeks, she was even less distractible, showed great eagerness in all experiments, attempting to manipulate the apparatus herself. Towards the end of this period she showed frequent violent

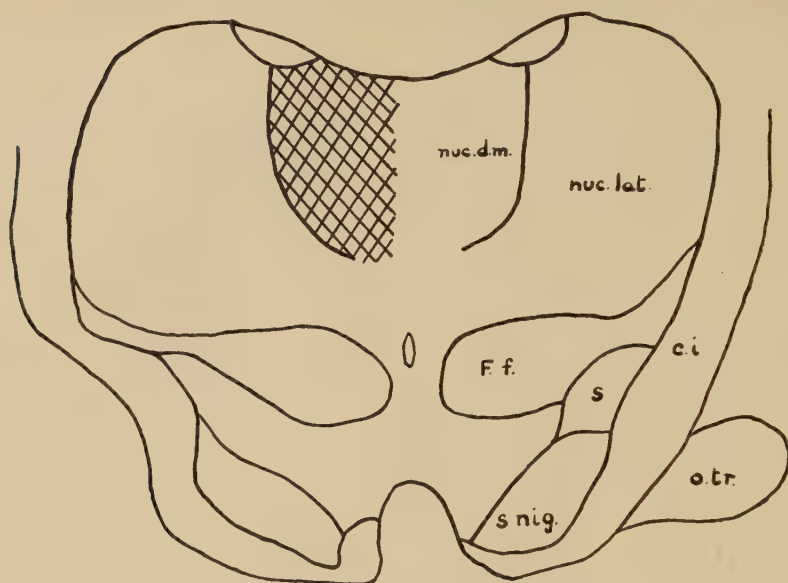


FIG. 4.—Diagrammatic representation of the unilateral lesion of the dorso-medial nucleus in M.D.M. 1.

agitations, and in the experimental situation was “too eager to stop and think.” She was highly excited by novel stimuli.

After five weeks there was a sudden change. She reverted to very gentle and tame behaviour, but became more distractible in experiments than previously. She was killed at six weeks.

(b) *Neuro-histological Findings*.—Many of the sections were studied successfully using Heidenhain's myelin stain. The right lesion extended more posteriorly than the left. Knife damage was seen in both sides of the corpus callosum, reaching the hypothalamic region on the right by cutting between the anterior nucleus and the nucleus ventralis anterior, damaging the mamillo-thalamic tract and entering the right paraventricular region. On the left the internal capsule, the globus pallidus and the left anterior nucleus were damaged. Both medial portions of the dorso-medial nucleus were heavily degenerated, particularly on the right side of the ventro-medial portion. This may have been partly due to connections with the damaged paraventricular region of the hypothalamus.

This lesion could be classed as a very posterior leucotomy since it severed fibres connecting the frontal lobe and the dorso-medial nucleus of the thalamus (shown by heavy degeneration in the latter).

Attempted Lesions on the Thalamus.—Four monkeys were used for these experiments (M.D.M. 1, 2, 3 and 4) but owing to severe haemorrhage into the third ventricle positive results were not obtained from M.D.M.4, which died six days after the operation, while the lesion in M.D.M.2 proved to be too far anterior, and this case has been classed elsewhere.

M.D.M.1 (Fig. 4). (a) *Behavioural Changes*.—Before the operation, this male rhesus was rather more timid and jumpy than the average. He would never accept food from strangers.

Immediately after the operation he appeared tamer, but at the end of a week he was showing signs of a returning timidity at taking food from outside the cage. He became more distractible, and would suddenly lose interest in a food-reward experiment (even when very hungry), jumping around the cage and vocalising. In general the animal remained fairly tame but there were occasional spontaneous outbursts of motor activity, and, in particular, sudden snatches and biting at the experimental equipment, especially when waiting, or after making an incorrect response to a test. He frequently gave the appearance of "not stopping to think" in choice-reaction experiments. This sort of behaviour persisted until 25 days after the operation, when the animal was killed.

(b) *Neuro-histological Findings*.—A well marked lesion was found in the medial portion of the left dorso-medial nucleus, from which fibres were seen passing through the lateral nucleus to the internal capsule, via the anterior medullary lamina.

The lesion involved the left fornix and this degeneration could be followed into the hypothalamus; the posterior commissure and habenular commissure were cut and there was marked degeneration of heavily myelinated fibres descending into the pons. The corpus callosum, supra-optic commissure, cerebral peduncles and gyrus cinguli showed degeneration, probably through direct injury in the latter. There was further degeneration showing one bundle of the mamillo-thalamic tract entering the medial nucleus in the centre, the other bundle forming the capsule. There was incidental degeneration in the stria of Lancisi and fibre degeneration of a coarse nature in the septal cortex, corresponding to the coarse degeneration seen in a caudal section at fornix level.

M.D.M.3 (a) *Behavioural Changes*.—Before the operation this male rhesus was co-operative and lively, and would frequently "steal" food from an observer. Occasionally he became distractible, and his reactions to an observer staring at him were similar to those of M.Th.L.13—mouth gaping, jerky movements and vocalising. At one time a female monkey in the next cage died, and he became subdued for a fortnight, after which the old liveliness returned.

Immediately after the operation he was lively and tamer, but two days after the operation a paralysis developed. At this stage he would go out of his way to be stroked, responding sexually. He made no overt responses to painful stimuli. Twelve days after the operation, the monkey appeared to have recovered, and his general behaviour was indistinguishable from that pre-operatively, except that changes of mood were more sudden, and that he was rather more distractible.

(b) *Neuro-histological Findings*.—The lesions made in this monkey were unfortunately too far posterior, in spite of the use of an elaborate technique. The misplacement was probably due to excessive forward tilting of the head resulting in the lesion being placed just above and anterior to the posterior commissure on the left and in the medial portion of the pulvinar on the right. There was much operational damage in the parietal cortex. The needle tracts could be seen clearly on both sides and there were obvious lesions in the fornix

and corpus callosum. A large number of cortico-pontine and cortico-spinal fibres degenerated, traceable in the internal capsule and in the region of the pons.

Within the thalamus the nuclei showing degeneration were the pulvinar, Forel's Field, and the n. ventralis lateralis; also several commissures showed clear fibre degeneration; the posterior commissure, the intercollicular commissure and the inter-thalamic commissure. An interesting fibre degeneration was seen in the hippocampus; such degeneration results from both frontal and angulate lesions. Particularly large fibres could be seen in the fasciculus thalamicus, passing into Forel's Field and from there reaching the posterior part of the hypothalamus. Owing to damage in the fornix, degeneration was found in the two mammillary bodies.

M.D.M.4.—Male rhesus. As the post-mortem examination showed that, apart from the ventricular haemorrhage, the operational procedure to produce a bilateral thalamic lesion was successful, a more detailed account of the operation will be given.

A rectangular bone flap was turned and the dura on both sides turned back to the mid-line. On either side four veins entering the superior sagittal sulcus were coagulated. After identifying the motor cortex the rotating knife was inserted on the left side 3 mm. in front of the central sulcus and the lesion effected. A similar procedure was used on the right side. The knife was moved further frontally after the first and second lesions and additional lesions on either side 5 mm. in front of the central sulcus were made. Unfortunately, after the fourth lesion a vessel of the choroid plexus of the third ventricle was cut, causing the interventricular haemorrhage.

The effects of the lesions and the haemorrhage proved to be so severe that the animal was killed after six days as he was unable to feed himself and had great difficulty in breathing.

When the brain was sliced extensive bilateral damage to both anterior and medial nuclei was found, so from this point of view the lesions were successful. Further attempts at using this procedure could not be made because of lack of material.

Psychological Test Results.

M.D.M.1 (Thalamotomy, extensive lesion of left D.M.N.) had a measurable memory-span 15 days after operation, but this disappeared by the 20th day; *M.Th.L.13* (complete bilateral leucotomy) had a measurable span at 21 days after the operation (of the same order as the pre-operational span), but this had disappeared by the 35th day; *M.D.M.2* (posterior leucotomy) had a measurable span at 15 days after the operation (of the same order again as the pre-operational span), and in this case the subject continued successfully to solve this test until its death. *M.D.M.3* (no thalamic nor prefrontal lobe damage) had a measurable memory span of a pre-operational order from 13 days after this operation until observation ceased four weeks later.

It is difficult to point to anything in the neuro-histological findings in *M.D.M.2* which might parallel this differentiation in behaviour from *M.Th.L.13* and *M.D.M.1*, except that only the medial parts of the D.M.N. were unequally

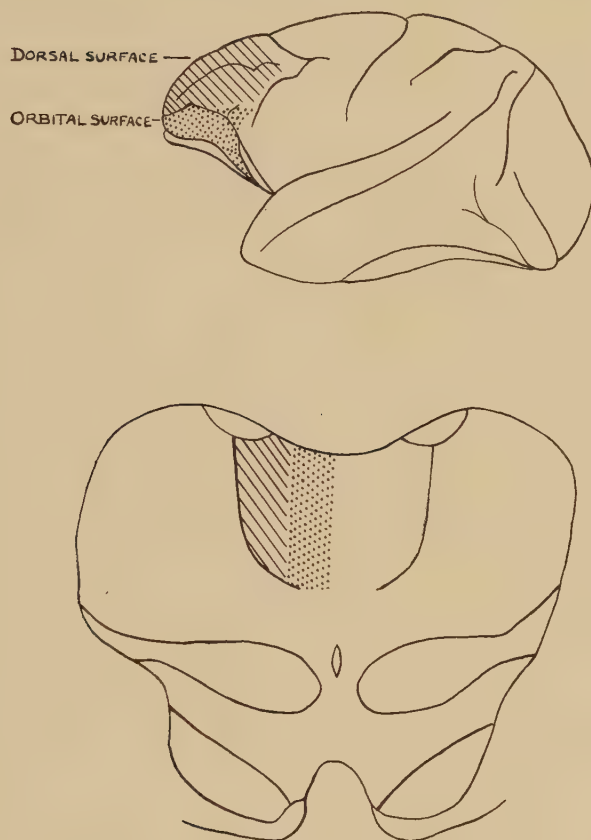


FIG. 5.—A composite diagram to illustrate the projection of the dorso-medial nucleus onto the dorsal and orbital surface of the frontal lobe.

involved in M.D.M.2. In the subject M.D.M.3 there was no involvement of frontal areas and no degeneration of the D.M.N.

The final deterioration of performance of M.D.M.1 and M.Th.L.13, and the occasional deterioration of M.D.M.2 all took the form of the persistent taking of one mug, despite continued lack of reward; in the cases of M.D.M.2 and M.Th.L.13, it was a mug for which preference had been shown also before operation, and the preference did not appear to depend on handedness. Before the operation M.D.M.3 tended to persevere on the right-hand mug. After the operation this was the one mug he tended to avoid.

These results indicate that:—

1. The inability after leucotomy or thalamotomy to perform delayed-reaction tests may not result directly from damage caused by the knife, but may depend more on subsequent degeneration.
2. A tendency to perseverative or stereotyped responses may be particularly characteristic of this period of deterioration.

Histological Findings.

See Fig. 5. They confirm previous observations by Le Gros Clark, Walker, Meyer, McLardy, and others.

COMMENTS.

*Behavioural Changes.**(a) Following Leucotomies.*

The maximum taming effect was achieved by a complete leucotomy in the coronal plane (M.Th.L.9) where the neuro-histological findings revealed that the orbital surface had been spared and only the lateral portion of the D.M.N. was found to be degenerated.

In the second, complete leucotomy (M.Th.L.13) taming was also marked, though less pronounced than in M.Th.L.9. Histological examination in this monkey revealed an encroachment of the lesions towards the orbital surface and a more complete degeneration of the D.M.N.

In the horizontal leucotomy motor hyperactivity followed for only two weeks after the operation, the histological study showed that the connections from the orbital surface had not been interrupted and only the lateral portions of the D.M.N. had degenerated. Following the bilateral leucotomy (M.Th.L.12) involving the lower orbital part of the prefrontal lobe motor hyperactivity was more marked and persistent. With damage to the orbital part of the frontal lobes the medial portion of the D.M.N. especially the pars magnocellularis was severely degenerated. Behavioural changes followed the posterior leucotomy (M.D.M.2) were less definite, in spite of a certain amount of hyperactivity alternating with gentle and tame behaviour. Here both medial portions of the D.M.N. were heavily degenerated, particularly on the right side.

(b) Following Thalamotomy.

After an extensive lesion of the left dorso-medial nucleus (M.D.M.1) the animal was persistently less active, especially marked during the first week following the operation, but occasional outbursts of motor hyperactivity occurred. In M.D.M.3, where the dorso-medial nucleus remained undamaged, the behaviour was indistinguishable from that shown pre-operatively already 12 days after the operation.

(c) Other Observations.

Most animals showed a tendency to revert to pre-operational personality at from two to five weeks after the operation. The marked exception to this was M.Th.L.9. This monkey was the only one to be taken out of its cage and led about.

The three animals observed in detail (M.D.M.1, 2, M.Th.L.13) all developed certain tendencies at about the third week after operation; these were (1) an "eager" attitude towards the tests, and the appearance of "not stopping to think." (2) Periodic outbursts of aggressive behaviour, usually directed at the experimental apparatus, and often occurring when the experimenter assumed the animal to be in a state of tension or suspense. (Not seen in M.D.M.3.)

There was some indication that these conditions became modified in time; however, none of these subjects was kept longer than 45 days after operation, and further modifications might have occurred.

DISCUSSION AND CONCLUSIONS.

In view of the fact that there were usually multiple lesions, only limited generalisations can be made.

The most marked state of apathy or taming having resulted from a complete leucotomy in the coronal plane where the orbital surface was spared confirms the results of Bard and Mountcastle (1947) in cats. Increased motor activity and aggressive behaviour following leucotomy was most marked when the orbital surface was involved in the lesion (thus confirming the work of Ruch and Shenkin on area 13), or when the medial parts of the thalamus, being the relay station of the orbital surface, were damaged in thalamotomy.

The psychological test results seem to indicate that the deterioration in memory span is dependent on the amount of white matter cut or the extent of the thalamic lesion. It was most marked following a complete leucotomy and absent where no involvement of the frontal areas and no degeneration of the D.M.N. was present. This confirms the view of Meyer and McLardy (1949) that there is a certain relationship between the degree of personality changes and the amount of prefrontal cortex cut. Whether it is of significance that deterioration was less marked when only the medial parts of the D.M.N. were involved as compared with the lateral ones remains to be confirmed.

The observation that deterioration in memory span and other behavioural changes like perseveration and stereotypies, tended to occur about three weeks following the operation may indicate that these changes do not result directly from damage by the knife but may depend on subsequent degeneration. Harlow et al. (1948) have reported a perseveration of a different kind following leucotomy. The observation that there is the same delay after leucotomy as after thalamotomy may suggest the prefrontal cortex or diencephalic structures as the seat of the degeneration necessary to produce these changes.

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ANATOMICAL COMMENTS ON PSYCHOSURGICAL PROCEDURES.*

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THERE has recently been a plethora of new methods of psychosurgery. This has, we believe, created considerable bewilderment in the minds both of the clinical psychiatrists who have to decide which of the methods to choose and of the neurosurgeons who have to practise them. The aim of the present paper is to clarify and disentangle the situation as far as this can be done from the anatomical angle.

The different operations may be divided into three groups: leucotomies, cortical ablations, and miscellaneous.

Within the first group, the leucotomies, one may usefully distinguish, at the one extreme, methods based only on external measurements; the wholly blind operations. These include the older orthodox methods of prefrontal leucotomy, still the most commonly used, and transorbital leucotomy. At the other extreme are the leucotomies under direct visual control; the open methods, such as the operation introduced by Lyerly (1939) and elaborated by Poppen (1948 *a, b*); McKissock's (1949) modification of it, a rostral leucotomy, and Scoville's (1949) method of undercutting which, as far as one can judge, should be very similar to McKissock's operation in its anatomical effect. In between the blind and the open methods may be placed certain devices such as the one advocated by Dax and Radley-Smith (1948) with approach from the temporal fossa and orientation by means of the blood vessels of the Sylvian fissure; then again, orientation by tapping the anterior horns with a ventricular cannula, by air ventriculography, or by post-operative contrast radiography.

The second group comprises the operations, all of them open, which entail resection of cerebral cortex. This may be total prefrontal lobectomy, as practised by Peyton and his associates (1948), or partial ablation as in Penfield's (1948) gyrectomy and in the topectomy of the Columbia-Graystone associates (Heath and Pool, 1948*a, b*; Pool, 1949), which has been adopted, with minor modifications, by several French neurosurgeons (Le Beau, 1948; Le Beau, Feld and Bouvet, 1948*a, b*; Feld and Messimy, 1949; Puech, 1949).

In the last group the most important method is thalamotomy, introduced by Spiegel and his associates (1947) and employed occasionally by Puech.

It is the *blindness* of the usual operation that must be held responsible for the unintentional variability in the surgical cuts so consistently demonstrated in our now large number of brains derived from leucotomised patients (Meyer and McLardy, 1949). Due allowance must be made, of course, for the fact that we tend to receive a high proportion of the surgical failures, for differences of technique employed by different neurosurgeons and for deliberate intention. We were actually able to eliminate these last two variables in the

* This paper was read by A. Meyer at the Annual Meeting of the Royal Medico-Psychological Association, on 22 July, 1949, in York.

case of, for instance, 21 brains operated on by the same neurosurgeon whose technique is highly standardised and whose skill is beyond question. He employs a cannulated leucotome to warn him if he trespasses upon the lateral ventricle—in which case he directs his instrument more rostrally before cutting. Yet in 10 out of the 21 cases the cut was so posterior, on at least one side, as to encroach upon structures posterior to the prefrontal region, whilst in two others the anterior horn was cut into within prefrontal precincts. That such cuts in too posterior a plane are dangerous was noted by Freeman and Watts as early as 1942, whilst the present writers (1948, 1949) have repeatedly shown how undesirable sequelae, such as restlessness, vasomotor and trophic lesions, persisting incontinence of urine, nutritional deficiency and respiratory disturbance, occur with significantly high frequency in cases with bilateral posterior cuts (i.e., cuts involving the posterior orbital region, the striatum and/or the premotor region), and seem to contribute to the occurrence of "delayed operative death" within five months of the operation.

From results of surgeons who have tried to improve the accuracy of the blind operation by other means, we can say that even preliminary location of the anterior horn by means of a ventricular cannula before inserting the leucotome is limited in effectiveness. Localisation of the anterior horns by means of a preceding air encephalogram might be more reliable, but although the method has been discussed, we have seen no published record of its systematic employment. Post-operative contrast radiography (by means of lipiodol, stainless steel wire or other contrast substance inserted into the cuts) still gives information only on the position of the cuts in relation to skull bearings, and, of course, only *post factum*. In a case* referred to us by Drs. Donovan and Galbraith and Mr. Jackson, an X-ray photograph (Fig. 1) was taken after a metal clip had been left in each cut. It showed the markers to be in front of the coronal suture. Dissection of the brain five months later showed that they were still situated in the leucotomy scars, but that these involved structures as far back as the putamen, one metal clip actually lying within putamen, internal capsule and caudate nucleus (Fig. 2). This is an example of the variability of the position of the coronal suture in relation to the underlying brain; a variability recently demonstrated impressively by Rowland and Mettler (1948).

Another interesting modification has been described by Dax and Radley-Smith, who approach the brain from the temporal fossa, gaining a limited orientation from the course of the blood vessels in the Sylvian fissure. These authors are satisfied that the procedure heightens the accuracy of the operation, but their method has not apparently been adopted by others; nor are pathological controls in sufficient numbers known to be available.

The foregoing considerations undoubtedly constitute some of the reasons why there has been such wide search for new methods—with outcome in thalamotomy, transorbital leucotomy, open leucotomy and cortical ablation.

Thalamotomy and transorbital leucotomy retain the defect that both are blind methods. *Thalamotomy* is performed by Wycis and Spiegel (1949)

* This case is included in a paper by Donovan, Galbraith and Jackson, since published in this Journal, July, 1949, 95, 655.

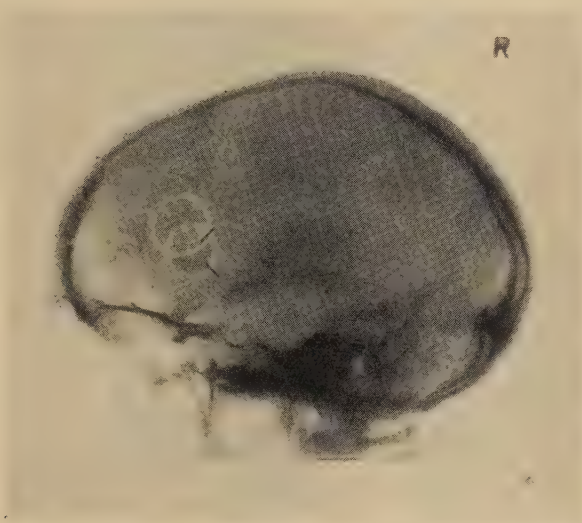


FIG. 1.—X-ray photograph, taken after operation, showing the position of the metal markers left in the leucotomy lesions.

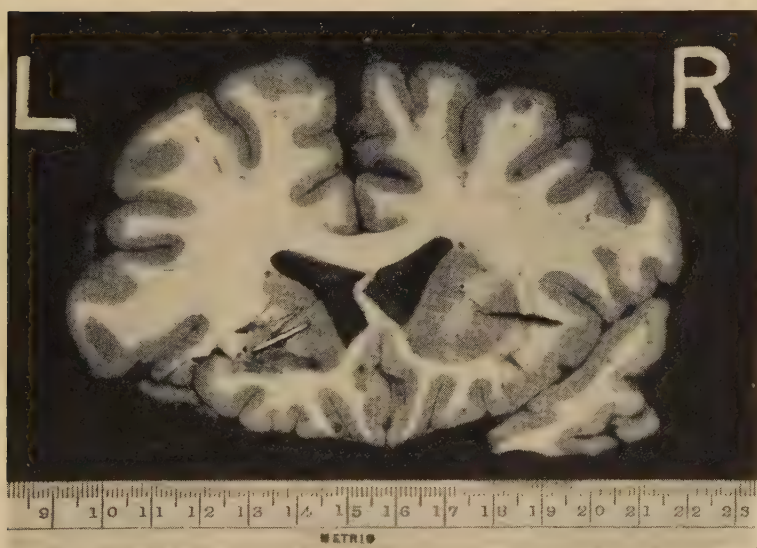


FIG. 2.—Position of the metal marker in the left leucotomy scar as seen after dissection of the brain.

with the help of a modified Horsley-Clarke instrument guided by prior location of the pineal gland by straight X-ray or air-encephalography. Even if it is possible to confine destruction with certainty to the dorsomedial nucleus, the parcellation of this nucleus in respect of its projection to the prefrontal cortex is such that even localised damage is liable to involve in addition the fibres projecting to a large part of the prefrontal region, thus rendering "individual

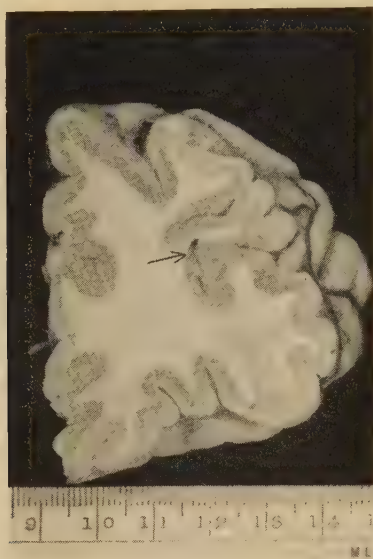


FIG. 3.—Punctate lesion (only) produced by the transorbitaly inserted leucotome : lesion in other hemisphere was identical.

dosage " difficult. The method is undoubtedly of no small theoretical interest. It should, among other things, enable a decision to be reached as to whether interference with the thalamo-prefrontal projection system alone is the all-important factor in psychosurgery of the frontal lobes; but those who advocate minimal localised interference will, we judge, find thalamotomy too diffuse.

The halo of novelty which surrounds *transorbital leucotomy*, and its technical simplicity, make one sometimes forget that this is still a blind operation and that—so far—the only published report on the actual extent of the lesion produced in the brain has been that of Freeman, in 1948, which was based upon a cadaver operation. Through the kindness of Dr. Walsh of Tone Vale Hospital we were able to study the extent of the cut in one of two patients who died of intercurrent disease several months after transorbital operation. The other case was investigated by Dr. Norman in Bristol, who told us that the damage was identical with that in ours (which he inspected). According to Dr. Walsh (who will probably publish these cases in detail)* the leucotomies were performed with the instrument recommended by Freeman. In both brains the entry mark of the instrument is to be seen clearly on each side, in a position slightly more anterior than in Freeman's cadaver specimen. Within the brain substance itself, inspection revealed only punctate lesions (Fig. 3) and nothing that could be interpreted as the result of a medio-lateral sweep, although Dr. Walsh assures us that such a movement was definitely carried out in the way demonstrated by Freeman. Whatever may be the explanation, these two brains undoubtedly demonstrate again that in blind operations there is liable to be unpredictable variation in the extent of the

* Now published in *Lancet*, 10 Sept., 1949, 2, 465.

lesions, the danger in transorbital leucotomy being of cutting too little and too anteriorly rather than too much and too posteriorly (at least in the "original" transorbital method as distinct from the new "deep cut"; Williams, 1949).

There remain for discussion the *open operations*, represented on the leucotomy side by the Poppen operation and on the resection side by Pool's topectomy. It is not always remembered that between leucotomy and resection there is a fundamental difference which may well have profound clinical significance, namely, that in the one only the fibres connecting with the nerve cells are severed, whilst in the other the nerve cells themselves are removed. It is known that the cortex anterior to leucotomy incisions remains histologically practically normal. The electroencephalogram after a period ranging from three weeks to three months (which probably covers the period of active repair) often returns to a relatively normal pattern. Potentially, therefore, this cortex may, by means of uncut fibres or pre-existing or newly-established subcortical or intracortical pathways, come under diencephalic influence again. This cannot happen when the cortex itself is removed. McLardy and Davies (1949) have discussed this difference in relation to the problem of relapse. It may well be that the ablation of prefrontal cortex, in sufficient amount, provides greater immunity from relapse than the mere cutting of its long fibre connections.

Poppen's open leucotomy consists in essence of a dorsal approach through a 2.5 cm. diameter trephine hole with its posterior brim bordering on the coronal suture, and bloodless cutting of white matter with a suction-cautery under direct illumination from a spatula fitted with a torch. From his recent impressive report on 470 operations (with only five deaths), and from personal descriptions by Mr. Falconer and Mr. McKissock, we have little doubt that this form of leucotomy offers a very large measure of precision and safety and, in addition, a maximum of flexibility in placing the cut according to the estimated requirements of the individual case. The rostral leucotomy of McKissock is, essentially, an anterior variation of Poppen's method, and has been devised to cut approximately the same anterior part of the prefrontal white matter as aimed at in transorbital leucotomy. Scoville has recently added another modification of the Lyerly-Poppen method by making the (dorsal) skull opening in a more anterior position, with its posterior brim 2 cm. in front of the coronal suture, and by abandoning suction and electro-cautery in favour of cutting.

Finally, circumscribed *cortical ablation*. This method commends itself to psychiatrists in virtue of its apparent cytoarchitectonic accuracy. This apparent accuracy, however, demands very considerable qualification from the anatomical point of view. The specific cytoarchitectural areas which it is the intention to ablate in topectomy are nicely mapped out in Brodmann's chart, but this and other charts commonly used take no account of individual differences, though the existence of such has been noted by various authors in the human brain and stressed in the macaque brain (Lashley and Clark, 1946). Moreover, the boundaries of the areas are by no means apparent in the brain on which the neurosurgeon operates, no matter how full the exposure. Nor are there any landmarks on the frontal lobe within reasonable reach of the

neurosurgeon which might enable him to deduce the position of the cyto-architectural areas. Even a precise frontal pole is oftener than not impossible to define on the flat frontal curve. Hence, other, indirect landmarks have been suggested. Le Beau and Puech and their associates describe how they determine the junction of areas 9 and 10 either by drawing a line to the convexity at right-angles to the Sylvian fissure, or by ascertaining the point which is 7 cm. from the coronal suture and 5 cm. from the "platform of the orbit" (see Fig. 3 of the paper by Le Beau, Feld and Bouvet, 1948a). We wish to stress that none of these landmarks is at all reliable. The substantial variability of the coronal suture in relation to underlying brain regions has, as already mentioned, been demonstrated very forcefully by Rowland and Mettler. It is very doubtful whether the slope of the Sylvian fissure, especially of the small fraction exposed, is of a consistency sufficient to warrant its use as a baseline. Even a slight aberration, or misjudgment, of it must lead to a formidable error in locating a point some 9 cms. distant along a perpendicular to it. The most reliable of the three landmarks appears to us to be the orbital plate, but, as we have confirmed in a number of skulls, the orbital plate slopes down some 2 cms. medialwards from its summit, and the French neurosurgeons do not state from what part of the orbital plate they took their measurements. (If one takes the level of the foramen caecum, situated at the junction of the crista gallica and the median ridge of the frontal bone, as a constant fixed bony point, the most antero-medial part of the frontal fossa, i.e., the tip of the cribriform plate of the ethmoid, lies about 1 cm. below it, and the summit of the orbital platform about 1 cm. above, and 3 cm. lateral to it.) Quite apart from the unreliability of these three landmarks, it has never been confirmed anatomically that any of them does in fact lead one to the desired cyto-architectural area of cortex.

In an attempt to obtain more reliable measurements we have begun to make systematic cyto-architectural investigations of the frontal lobes in normal brains, and give below a summary of our results so far in six hemispheres. These results, it must be emphasised, do not yet meet statistical requirements for validity, but they at least amplify the present scanty data furnished by Brodmann and others. For the purpose of this investigation we have divided the medial half of the frontal lobe into three sagittal blocks. Block III is the most medial, Block I the most lateral, and in between lies Block II (about $1\frac{1}{2}$ cm. from the mesial surface) from which the diagram in Fig. 4 has been made. In view of Lashley and Clark's warning that swelling and shrinkage may be so formidable and variable as to lead to considerable error if unheeded, each brain was measured fresh as well as at the end of fixation, and all measurements from stained sections corrected (as in this diagram) so as to apply to the size of the fresh brain as seen by the surgeon. As the fixed point from which to take the measurements we chose the point on the frontal pole* which is at the level of the foramen caecum.

* This point on the frontal pole was determined in the six hemispheres without knowledge of the skull data. As has been mentioned it lies one centimetre above the tip of the cribriform plate. Since the latter in turn corresponds with the tip of the olfactory bulb, the point one centimetre ahead of the olfactory bulb on the fresh isolated brain gives the position of our fixed point. We have had opportunity to check this fact at post mortem in two brains.



FIG. 4.—Normal 1. Right hemisphere. Projection diagram of sagittal block II showing the surface length of each Brodmann/von Economo area. The level of the foramen caecum in this particular block coincides with the junction of areas 10 and 11. ($\times 9/10$ original size.)

In the hemisphere represented in the diagram the sagittal surface distance from the level of the foramen caecum to the junction of areas 9 and 10 is 31 mm., from there to the beginning of dysgranular area 8 is 39 mm.; from area 8 to the beginning of agranular area 6 is 10 mm.; and from there to area 4 is 45 mm. On the orbital surface the distance from the fixed point to the end of the granular portion of area 11 is 33 mm.; then follow 7 mm. of dysgranular transitional cortex and 23 mm. of agranular cortex, now known as area 13. It will be noticed that the distance of 31 mm. from the level of the foramen caecum to the junction of areas 9 and 10 is some 2 cm. less than the measurement used by Le Beau and Puech. This might be partly due to the French surgeons, as already mentioned, taking their measurements in a more medial plane where the frontal fossa sinks 1 cm. below the foramen caecum. In Table I, showing the measurement of this distance in each of the three blocks in all six hemispheres, values more approximating to 5 cm. do in fact, occur in the third (*i.e.*, most medial) block. This same table shows that individual variations in the position of the junction of areas 9 and 10 are quite considerable, differing even within the more constant medial Block III by as much as 2 cm. (*i.e.*, 37 per cent. in Left hemispheres and 38 per cent. in Right hemispheres).

These individual differences are not confined to the position of the junction of areas 9 and 10. In the graph shown in Fig. 5 we have tried to bring out the individual variation, as well as left-right variation in these three normal brains, by expressing the sagittal surface length of each area in proportion to a total frontal cortex of 200 mm. length, and by relating them to the foramen caecum

TABLE I.—*Sagittal surface length (shown in mm.) of the dorsal portion of area 10/FE (i.e., from the level of the foramen caecum to the junction with area 9/FDm).*

	LEFT.	Maximal Individual Variation in %.	RIGHT.	Maximal Individual Variation in %.
Normal 1—				
Block I ..	..	38	28	
Block II	..	40	31	
Block III	..	31	31	
Normal 2—				
Block I ..	..	27	42	(I) 38%
Block II	..	37	51	(II) 39%
Block III	..	—	50	(III) 38%
Normal 3—				
Block I ..	..	33	26	
Block II	..	48	31	
Block III	..	49	50	

as baseline. That there are considerable differences in which all granular regions participate, both as between left and right and different individuals, is obvious. It is also clear that in some instances area 10 is totally or almost totally dorsal to the level of the foramen caecum, whilst in others it extends considerably ventral to it on to the orbital surface. It may be added that in all six hemispheres the granular cortex was found to extend more posteriorly in Block II than in either (the lateral) Block I or (the medial) Block III. This is in agreement with both Brodmann's and von Economo's findings.

These individual differences have, so far, been investigated only in respect of the antero-posterior length of areas. It may well be that the differences would be found reduced or exaggerated if full investigation in other diameters were carried out. Again, as Lashley and Clark and others have pointed out, the architectural differences within the granular prefrontal cortex are not so striking as to preclude considerable subjective errors in delineation. In an attempt to minimise this difficulty all the cytoarchitectural measurements have been checked independently by two of us. The subjective differences in parcellation encountered would not seem sufficient to explain away the differences shown in the graph. A much larger material, now under investigation, is, however, necessary to render the differences statistically valid. At present all that is intended is to demonstrate that any claim by surgeons that specific areas have been removed is a far from accurate statement. No matter how precise his bony landmarks or his electrical definition of agranular cortex, the surgeon can never tell the extent of granular areas 9, 10, 11 and 46, in any particular brain, or hemisphere. Some of the surgeons performing topectomy are well aware of this, but cytoarchitectonic pseudo-accuracy has had a considerable appeal to a wider psychiatric public, particularly because it has been employed in the concept of localisation of mental function. Kleist's well-known map is now recognised to be too atomistic, but his influence is

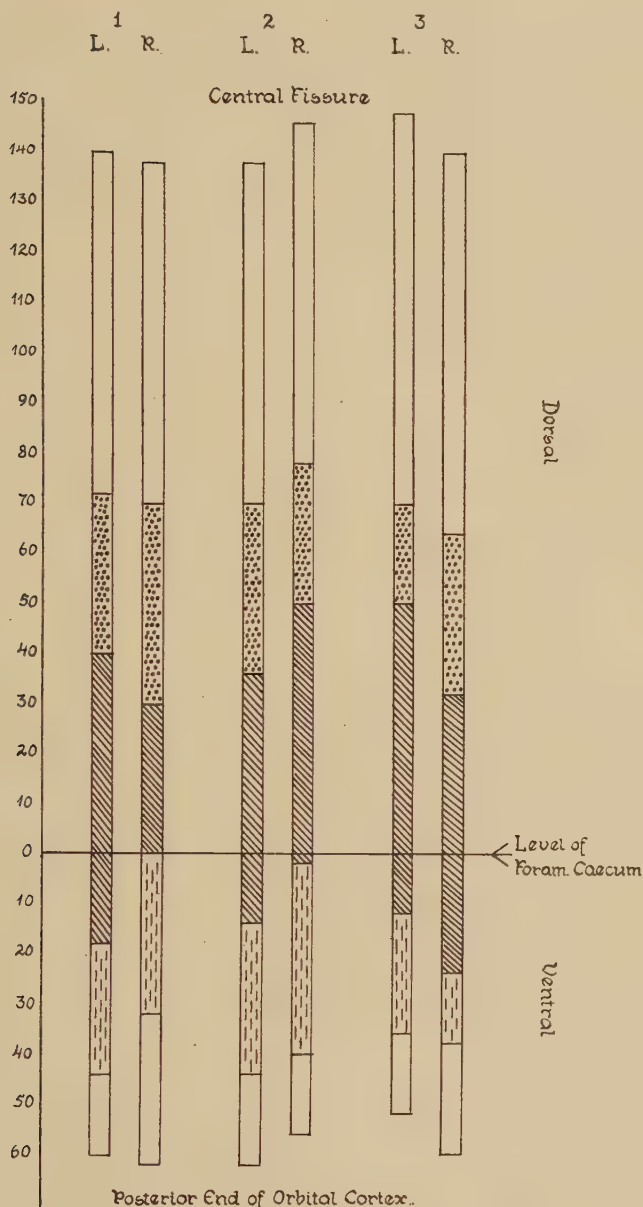


FIG. 5.—Graphic Representation of Individual Variation and of Left/Right Variation in Three Normal Brains.

(Expressed in proportion to a total frontal cortex of 200 mm. length, which approximates the absolute length in all cases.)

Area 10/FE = Area 9/FDm = Area 11/FF =

FDC
Agranular + dysgranular areas =

still alive. Our own studies of the problem (Meyer and McLardy, 1949; McLardy and Meyer, 1949) point to a slight preponderance of the orbital region in causing personality change and improvement, but apart from this we found in our anatomical material of over 60 cases with adequate survival, little encouragement for a rigid localisation of lesions in respect of either personality change or of clinical improvement. Several of our cases with the euphoric type of personality change had bilateral orbital damage, but others with typical fatuous euphoria had cuts which excluded these regions. Conversely, although several cases with the akinetic type of personality change had bilateral dorsal cuts, many others with such a personality change had no involvement whatever of the dorsal segments. These findings suggest that it is not so important that specific areas be removed, as that the amount of prefrontal cortex ablated be sufficient for the estimated requirements of the individual patients.

TABLE II.—*Sagittal surface length (shown in mm.) of granular and agranular frontal regions (c.f. Fig. 4).*

	LEFT.				RIGHT.			
	Ventral Agranular	Ventral Granular	Dorsal Granular	Dorsal Agranular	Ventral Agranular	Ventral Granular	Dorsal Granular	Dorsal Agranular
Normal 1 ..	16	44	71	65	30	33	70	68
Normal 2 ..	18	44	71	68	15	40	78	64
Normal 3 ..	16	34	68	73	20	36	62	71

The most important point is that agranular and even dysgranular cortex be not infringed upon, because, as we have mentioned earlier, undesirable sequelae appear to depend much on the involvement of the agranular cortex, perhaps because it is so much concerned with autonomic control. In Table II we have set out the sagittal surface length of the granular and agranular—plus—dysgranular dorsal and ventral frontal cortex in the six normal hemispheres. In the case of granular cortex measurements were taken from our “fixed point.” There are again individual differences, although not of the same magnitude as the variations within the granular frontal cortex. The lowest figure for granular cortex so far on the convexity is 62 mm.; on the orbital surface 33 mm. That is to say, ablations within these figures would, if our figures were statistically valid, be entirely safe in the average adult brain. These figures, it should be noted, are considerably smaller than those estimated by Le Beau and Puech, but agree better with Pool’s (1949) most recent measurements. The usual topectomy cut does not extend down to the orbital surface. It might well be worth exploring whether inclusion of its anterior half might not improve the results. Previous disappointing results with exclusively orbital ablations might be due to the fact either that the lesions infringed upon dysgranular cortex within the posterior half of the orbital region, or that the total amount of prefrontal cortex removed was simply too circumscribed.

In conclusion, there is a definite tendency away from the blind and extensive leucotomies towards operations carried out under full vision and restricted in size and position according to the estimated requirements of the individual case. Anatomical considerations have had a considerable formative influence

on this development. The two types of operation which in our opinion deserve an extensive trial are, firstly, leucotomy under full vision as practised by Poppen, Scoville and McKissock, and secondly, topectomy of granular frontal cortex. The fundamental difference between the two types of operation is that the one is a cutting of white matter fibres, the other a removal of cortical grey matter. This difference may or may not prove to be of clinical significance. The cytoarchitectural accuracy of the topectomies, often said to be their chief asset, has to be considerably qualified in the light of recent architectonic studies, including our own preliminary results.

SUMMARY

The various psychosurgical operations are classified and reviewed from the anatomical angle.

The two types of operation most deserving of extensive trial are considered to be leucotomy under full vision and topectomy of granular frontal cortex.

The inaccuracy of cytoarchitectural topography is demonstrated by the variabilities shown within the frontal lobes of six normal human hemispheres so far investigated by the authors.

The foramen caecum is suggested to be a relatively reliable fixed point from which to take rostral cortical measurements.

ACKNOWLEDGMENTS

The authors wish to acknowledge again their indebtedness to all those who have furnished the material on which this paper is based, and in particular to Drs. Donovan, Galbraith and Jackson for the X-ray photograph, to Dr. Walsh for permission to quote his two cases of transorbital leucotomy, and to the Curator of the British Museum of Natural History for facilities to make large-scale skull measurements.

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BODY SIZE, PERSONALITY AND NEUROSIS.

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FROM time immemorial man has tended to classify his fellow beings into physical types associated with specific disease susceptibilities or characteristic mental or moral qualities. The ancient Hindus described three types of human physique likened to the elephant, the bull and the deer. Hippocrates formulated a dichotomy in build with a narrow type, the habitus phthisicus as one extreme and a broad type, the habitus apoplectic, as the other.

Subsequently, various aspects of physical constitution have formed the basis of categorisation of physique. Thus humoral theories governed the classification of Galen whose doctrines of a humoral basis of disease susceptibility dominated medical thought for many centuries.

Functional concepts governed the classification of Rostan's (1828) Digestive, Muscular and Respiratory-cerebral types and Mills' (1917) Hypersthenic, Sthenic and Asthenic types.

Disease susceptibility governed the classification of Beneke (1878) who described Rachitic, Carcinomatous, Scrophulous and Phthisal physical types, and Draper (1925) with his Gall bladder and Ulcer types.

Bodily configuration was used as a primary basis for classification by Stockard (1923) and his Lateral, Intermediate and Linear types, Aschner (1924) with Broad, Narrow and Slender types; MacAuliffe (1925) with Round and Flat forms of physique; Weidenreich's (1926) Euryosomes and Leptosomes; Brugsch's (1931) Wide-chested, Normal-chested and Asthmatic types. Developmental Concepts governed the classification of Viola's (1919) Macro-splanchnic, Normosplanchnic and Microsplanchnic types, Von Rohden's (1928) Endodermic, Mesodermic and Ectodermic types and finally Sheldon's (1940) Endomorphic, Mesomorphic and Ectomorphic types designated according to the relative development of structures from the three primary germinal layers.

In the above rather bewildering variety of classifications of human physique, widely differing concepts have determined the choice of physical attribute as a basis for classification. In many the choice has been arbitrary and in others based on impression or unverified hypotheses.

In fact, it is only in recent years that satisfactory, scientific inductive methods of analysis have been applied to the study of variation in physique.

INDUCTIVE APPROACH TO THE STUDY OF BODY BUILD.

Classification is clearly desirable in order to reduce the manifold individual physical differences to some degree of order. Scientifically the only acceptable basis for classification will be that arising from induction.

A scientific inductive analysis of body build would involve :—

1. Collection of data on physique from a random sample of the population.
2. The measurement of the co-variation or correlation of all the physical data in the group.
3. The determination of the most succinct method of describing the variations in body build.

The statistical technique of Factorial Analysis, which had been used with success in the study of intelligence, affords a highly satisfactory scientific inductive procedure capable of application to the study of the variations in body build. It was first used in the study of body build by Burt (1938) and subsequently by his pupils Cohen (1938, 1940 and 1941), and Hammond (1942) on samples of different ages and racial composition. Rees and Eysenck (1945) applied Factorial Analysis to the study of body build in 200 soldiers and Rees (1949) in a group of 200 service women.

The results of factorial studies of physique show a general agreement in the elicitation of factors responsible for the variations in body build. The following are the main factors concerned :—

1. General Factor.
2. Type or Group Factors.

The general factor is a factor determining body size or bulk as opposed to bodily proportion or physical type in the customary sense of the term.

The type factor is bipolar, having positive correlations with length measurements and negative correlations with breadth, width and circumferential measurements. The type factor is therefore responsible for the existence of two antithetical types of body build, the relatively broad and the relatively slender (Euryomorphic and Leptomorphic types of Rees and Eysenck, 1945).

GENERAL FACTOR OF BODY SIZE.

The majority of typological classifications deal with bodily proportion rather than size, and the factor of size has been neglected in the fields of constitutional medicine and psychology.

The size factor of body build in fact accounts for two to three times as much of the variance in physical measurements as the type factor (Rees and Eysenck, 1945). The existence of a general factor underlying the variations in bodily dimensions has now been demonstrated in children of both sexes and of various ages and in adults of both sexes and differing racial composition. Carter and Krause (1936) analysing the data of Bakwen and Bakwen (1934) on neonates found that all measurements were positively correlated indicating the presence of a general factor of growth.

McCloy (1940) in a study of growth in groups of different ages ranging from birth to maturity found a factor influencing general growth in all dimensions in all the groups studied.

Mullen (1940) in a factorial study of anthropometric data of groups of girls of age 7-15, found the presence of a general factor in all groups.

Burt (1937) in a factorial study of British children discovered a general

factor as well as type factors, and in 1944 reported similar factors in American youths elicited from a factorial analysis of the data of the Harvard growth study.

Cohen (1938, 1940 and 1941) in factorial studies of adolescents and Jewish adults of both sexes found general as well as type factors underlying the variations in physique.

Rees and Eysenck (1945) carried out a factorial analysis of 17 bodily measurements in a group of 200 soldiers and elicited two main factors, i.e., a general factor of body size and a type factor determining physical proportions.

Rees (1949) in a factorial study of anthropometric measurements in 200 women A.T.S. discovered a general growth factor as well as a well defined type factor.

The discovery of a general factor in all the above studies in widely differing groups indicates the universality of such a factor underlying the variations in human physique.

It is interesting to note that Huxley (1932) has described two main types of growth in animals which correspond to the general and type factors elicited by factorial analysis, viz. :—

1. General or isogonic.
2. Differential or heterogonic.

Table I gives the first factor saturation and coefficient of variation of the anthropometric data studied by Rees and Eysenck (1945). The correlation

TABLE I.—*First factor saturations and coefficients of variation of anthropometric measurements on 200 soldiers.*

First factor saturation.				Co-efficient of variation.	
Stature	..	..	..	·73	3·9
Suprasternal height		..	..	·82	4·1
Symphysis height	..	..	..	·69	5·5
Breadth of skull	..	..	..	·31	4·3
Length of skull	..	..	..	·25	3·3
Biacromial diameter	..	..		·71	4·3
Transverse chest diameter			..	·67	6·6
Sagittal chest diameter	..	..		·65	6·5
Bicristal diameter	..	..	..	·77	5·9
Trunk length	..	..	..	·41	4·6
Sternal length	..	..	..	·41	5·6
Chest circumference at inspiration				·54	3·7
Chest circumference at expiration	..			·54	5·01
Weight	..	..	..	·64	10·8

between first factor saturation and coefficient of variation was found to be +·29 with a probable error of 0·16 and is therefore not statistically significant.

Table II gives the general factor saturations of anthropometric measurements on a group of 200 adult women students (Rees, 1949), together with those of Mullen's (1940) investigation. Mullen's choice of anthropometric measurements

TABLE II.—*First factor saturations of anthropometric measurements on female groups of varying ages.*

Variable.	200 adult women (British) (Rees, 1949).	Groups of girls age 7-17 (American) (Mullen, 1940).					
Age		7	9	11	13	15	17
Stature	·71	·87	·84	·88	·77	·69	·62
Arm length	·68	·75	·79	·85	·66	·59	·50
Weight	·86	·83	·76	·78	·75	·69	·76
Bicristal diameter ..	·56	·67	·66	·73	·66	·55	·46
Chest circumference ..	·73	·68	·58	·75	·50	·56	·60
Transverse chest dia. ..	·54	·59	·54	·62	·60	·59	·67
Sagittal chest diameter	·68	·52	·46	·55	·43	·40	·35
Biacromial chest dia. ..	·67	·70	·62	·68	·69	·58	·70
Head length	·36	·39	·48	·40	·44	·33	·41
Head breadth	·11	·35	·24	·23	·28	·38	·21

were similar to ours and the measurements corresponding most closely are shown in the table. The rank difference correlation between the average first factor saturation of the traits of Mullen's groups and ours is ·644 with a P.E. of ·126. This statistically significant correlation between the first factor saturations of our adult female group with the younger age groups of Mullen indicates consistency considering the fact that the populations were widely divergent, not only in age, but in racial composition and probably socio-economic status, and also in that the measurements were taken by different observers not necessarily using identical anthropometric techniques.

This would seem to give further indication of the existence of underlying general factor of growth to which our statistical factor is at least a useful approximation.

Scientific enquiries on body size and its psychological correlates are almost non-existent. Sheldon (1927), however, in a study of the correlation of body build as measured by the morphological index of Viola and ratings of aggressiveness, leadership and sociability, found that bigness showed a definite though low correlation with all three traits.

In view of the statistical importance of the general factor it was decided to carry out an investigation of the relationship of body size (as opposed to physical proportions) to personality and neurosis in a group of soldiers at Mill Hill Emergency Hospital, London.

Preliminary reports (Eysenck, Himmelweit and Rees, 1947) indicated the need for a more detailed study. The first problem was to find a convenient index of body size. The relevant data for constructing an index of body size are given by the first factor saturations of the anthropometric measurements (Table I). The following measurements were found to have the highest degree of saturation with the general factor of body size, and therefore likely to be the most useful measurements for inclusion in body size indices.

1. Suprasternal height.
2. Bicristal diameter.
3. Stature.
4. Transverse chest diameter.

Stature and transverse chest diameter were chosen as these measurements had been taken on a group of 1,115 soldiers successively admitted to Mill Hill Emergency Hospital on whom detailed psychological data was also available.

The product of these two measurements gives a convenient index of body size. The mean stature was 72.067, standard deviation 6.69, and coefficient of variation 3.88, and the mean transverse chest diameter was 27.63, standard deviation 1.902 and coefficient of variation 6.89.

It will be seen that the coefficients of variation of these two measurements differ widely, and therefore the absolute measurements could not be used for inclusion in an index of body size.

Each measurement was therefore converted into standard measure, i.e., expressed in terms of standard deviation, and on each patient the product of stature and transverse chest diameter in standard measure was calculated.

FREQUENCY DISTRIBUTION OF BODY SIZE INDEX.

Fig. 1 shows the distribution of the body size index in a group of 1,000 soldiers who were neurosis patients successively admitted to Mill Hill Emergency Hospital, London.

It will be seen that the index values are distributed along a normal frequency (Gaussian) curve with some positive skewness. The frequency curve shows

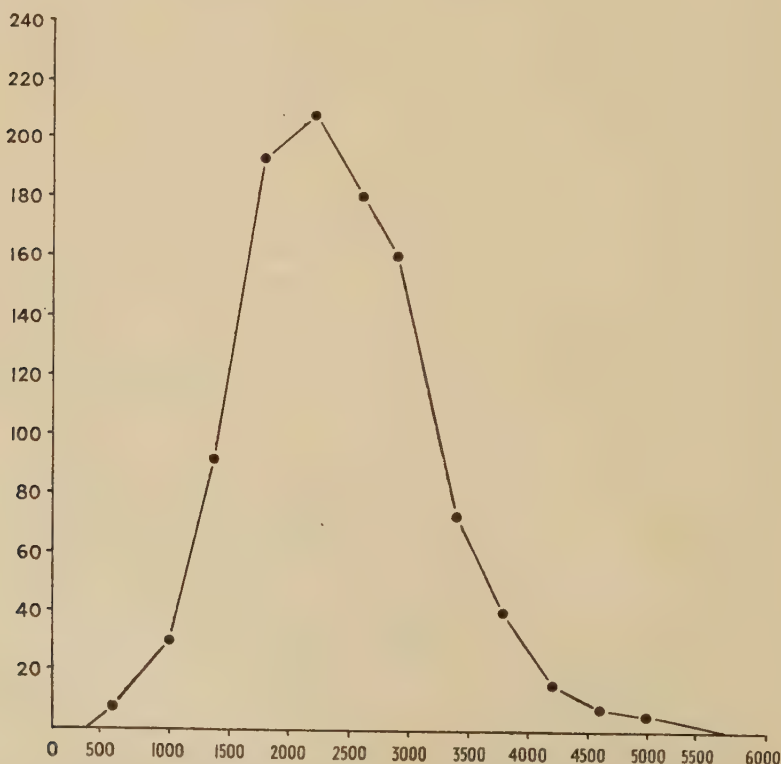


FIG. 1.—Frequency distribution curve of the body size index in a group of 1,000 soldiers.

no evidence of bimodality or multimodality which would suggest the existence of disparate types of body size but a continuous variation from one extreme to the other.

For the purposes of the investigation it will, therefore, be necessary to choose arbitrary points for classification of the group. The demarcation points chosen were one standard deviation above and below the mean dividing the group into three classes.

1. Small size. *Microsomatics*, individuals with index values of 1,683 and less.
2. Medium size. *Mesosomatics* comprising individuals with index values between 1,684 and 3,110.
3. Large size. *Macrosomatics*, individuals with index values of 3,111 and over.

On each patient an item sheet had been completed containing over 200 items relating to social data, personal and family history, personality, symptomatology, etc. An item analysis was carried out for the microsomatic, mesosomatic and macrosomatic groups, and the percentage distribution of the more important traits is shown in Tables III-VI.

RESULTS.

The significance of the difference in percentage incidence between the groups was tested by the critical ratio method and only ratios of 2 and over were taken as significant.

INTELLECTUAL STATUS.

The results indicate that the microsomatic group is of a lower level of intellectual capacity, as shown by the significantly higher proportion of individuals of below average intelligence in both perceptual (matrices) and vocabulary tests (Table VI). Further evidence of a lower intellectual level in the microsomatic group is the higher proportion of individuals who failed to go higher than Standard V in school and the higher proportion of individuals with unskilled civil employment (Table III).

PERSONALITY.

The microsomatic tend to be of inadequate personality make-up, as shown by the higher incidence of weak, dependent, anxious and hypochondriacal types of personality, with narrow interests and hobbies.

The macrosomatics showed, in addition to greater body size, better muscular tone and posture. From the point of view of neurotic constitution the macrosomatics are also predisposed, as shown by the high incidence of childhood symptoms, a clear disposition to mental illness and high proportion of individuals rated as having an unstable personality. The predisposition to neurosis in macrosomatics expressed itself differently from microsomatics in that they tended to be more active, rebellious and aggressive.

TABLE III.—*Social data and history.*

	Microsomatics (156).	Mesosomatics (688).	Macrosomatics (156).
	%	%	%
<i>Age—</i>			
16-20	47.7	7.3	3
21-25	25.6	25.4	26.9
26-30	25	28.3	30.1
31-40	37.2	34.7	36.5
41 years +	4.48	4.2	3
<i>Modal civilian occupation—</i>			
Unskilled	50.6	38.3	39.1
Semi-skilled	30.1	37.6	30.1
Skilled	12.1	20.5	23.7
Administrative or Profes- sional	5.8	4.5	4.5
Unduly frequent changes of employment	10.25	6.7	7.1
<i>Civil state—</i>			
Married	55.8	65.8	62.8
Engaged	1.3	2.5	1.3
Single	37.1	26.2	30.1
<i>Sexual activity—</i>			
Normal	73.7	80.7	76.3
Inhibited	17.3	11.2	8.9
Subject to worry	10.3	8.4	12.8
<i>Education—</i>			
Elementary-poor	26.3	21.7	16.7
Elementary-good	58.9	63.1	59.6
Secondary or Central	12.2	13.8	21.2
Higher	2.5	1.5	2.6
<i>Past Physical health—</i>			
Good	44.2	51.7	37.2
Medium	48.1	45.2	57.7
Poor	7.7	3.1	5.1
<i>Alcohol consumption—</i>			
Teetotal	53.8	51.7	37.1
Moderate	44.2	45.2	57.7
Excessive	1.9	3	5.1
<i>Family history—</i>			
Negative	12.8	11.4	12.2
Psychosis	5.1	4.9	6.4
Epilepsy	1.3	2.3	0.6
Mental deficiency	26.9	31.4	32.7
Pronounced neurosis	26.9	15	14.7
Slight neurosis	44.9	48.7	48.7

TABLE IV.—*Personality and previous mental health.*

				Microsomatics.	Mesosomatics.	Macrosomatics.
				%	%	%
Unstable	..	..	..	45.5	48.8	52.6
<i>Hobbies—</i>						
Broad	..	..	..	23.1	24.7	34.6
Narrow	..	..	..	76.9	75.3	65.4
<i>Drive and energy—</i>						
Inert	..	..	..	25.6	27.2	18.6
Average go	..	..	..	69.9	69.3	75.6
Conspicuous energy	..	..	..	4.5	3.5	5.8
<i>Delinquent</i>	..	..	..	5.8	4.7	5.1
<i>Rebellious and aggressive</i>	..	..	..	8.3	4.4	10.9
<i>Weak, dependent</i>	..	..	..	57.7	49.7	37.8
<i>Touchy, suspicious</i>	..	..	..	29.5	31.1	33.9
<i>Cyclothymic—</i>						
Somewhat	..	..	..	26.3	28.5	27.6
Very	..	..	..	3.2	2.5	1.3
Schizoid	..	..	..	26.3	33.3	31.4
Hysterical	..	..	..	21.2	24.3	21.2
Anxious	..	..	..	60.1	62.9	50.6
Hypochondriacal	..	..	..	26.9	32.7	16.7
Obsessional	..	..	..	22.43	24.7	22.4
Symptoms in childhood	..	..	..	44.2	39.7	37.2
Clear predisposition	..	..	..	34.6	34.3	38.5
Definite illness	..	..	..	5.8	6.4	5.1

MENTAL STATUS.

Symptomatology and diagnosis showed a general agreement in the three groups. Notably the microsomatics had a significantly higher incidence of depression as a symptom.

The mesosomatic group usually occupies an intermediate position in the percentage incidence of those traits showing statistically significant differences.

DISCUSSION.

The general picture that emerges is that those neurotics of small body size tend to be weak, dependent, anxious, hypochondriacal, and generally inadequate in personality, whereas neurotics of large body size tend to show more active though unstable personalities with better musculature, higher intellectual level and a better prognosis for return to military duties.

These findings are what one might expect on general considerations. The small person, apart from his constitutional make-up (i.e., his physical psychological and physiological attributes determined in the main genetically) might react in many ways to his smallness, as indicated by Adler. The person may overcompensate for his smallness by assuming aggressive and dominating

TABLE V.—*Present illness.*

				Microsomatics.	Mesosomatics.	Macrosomatics.
				%	%	%
AETIOLOGY.						
<i>Physical causes—</i>						
Unimportant	..	..		66·	68·6	64·1
Precipitating	..	..		21·1	20·1	25·6
Important	..	..	..	12·2	10·2	10·9
Dominant	..	..	..	4·5	2·6	6·4
<i>Psychological causes—</i>						
Unimportant	..	..		5·8	5·	7·7
Precipitating	..	..		17·9	16·9	17·9
Important	..	..	..	39·1	40·	44·2
Dominant	..	..	..	54·5	51·6	48·7
Stress of bombardment or exposure	..	..	..	20·5	26·5	25·0
War-time separation, regimentation	..	..		50·6	58·1	53·2
Unsuitable work	..	..		17·9	15·4	16·7
Domestic problems	..	..		26·9	33·4	30·1
<i>Duration of illness before admission—</i>						
0-3 months	..	..	..	6·4	4·7	4·5
3-6 months	..	..	..	11·5	10·6	13·5
6-12 months	..	..	..	16·	19·5	18·6
1 year +	..	..	..	66·	65·1	63·5
<i>Exposure to enemy action—</i>						
Slight or none	..	..	..	60·8	54·9	51·3
Medium	..	..	..	19·2	22·5	19·9
Severe	..	..	..	19·9	22·5	28·8

traits or he may accept with a more normal degree of compensation or he may react by developing feelings of inadequacy or inferiority.

From the results of our study we find little evidence that neurotics of small body size tend to overcompensate by aggressive or dominating behaviour. It might be argued that a socially acceptable degree of compensation in this direction might have a salutary effect in preventing neurosis. In fact we find evidence of anything of the opposite tendency, i.e., acceptance with feelings of inferiority as shown by the high incidence of weak, dependent and timorous personalities (53 per cent.), anxious highly strung types of personality (61 per cent.), hypochondriacal tendencies (27 per cent.), and the lack of such possible signs of overcompensation such as rebellious and aggressive tendencies (13 per cent.), or conspicuous energy and activity (4·5 per cent.).

While it is clear that there is little evidence of overcompensation for any feelings of physical inferiority in the microsomatic group, it would not be safe to assume that lack of such compensation and the adoption of a defeatist

				Microsomatics (156). %	Mesosomatics (688). %	Macrosomatics (156). %
Somatic anxiety	..	..	..	53·8	48·8	53·8
<i>Headache—</i>						
Mild	..	..	..	46·8	47·5	42·9
Severe	..	..	..	12·8	13·8	10·9
Lassitude, fatigue	..	..	..	53·2	51·3	50·1
Dyspepsia, vomiting	..	..	..	18·6	14·8	13·5
Fainting	..	..	..	14·7	11·5	14·1
<i>Pain not demonstrably organic</i>						
in origin	..	..	..	18·0	23·7	22·4
Tremor	..	..	..	30·1	25·	26·9
Stammer	..	..	..	·6	9·4	7·7
Enuresis	..	..	..	3·2	2·9	2·6
Sexual anomalies	..	..	..	12·8	13·5	15·4
Anxiety	..	..	..	85·9	83·0	94·4
Depression	..	..	..	71·8	90·0	58·3
Paranoid	..	..	..	0	·6	1·3
Elation	..	..	..	0	·6	1·3
Irritability	..	..	..	30·1	31·7	38·5
Apathy	..	..	..	21·2	31·7	19·9
<i>Hypochondriasis—</i>						
Mild	..	..	..	19·2	25·6	23·1
Moderate	..	..	..	12·2	10·6	8·3
Severe	..	..	..	1·3	1·7	1·3
Hysterical attitude	..	..	..	28·8	33·4	28·8
Depersonalisation	..	..	..	2·6	1·5	4·5
Hysterical conversion	..	..	..	23·1	29·4	22·4
Symptoms	..	..	..	10·3	5·7	3·8
Obsessive-compulsive	..	..	..	2·6	6·4	7·1
<i>Muscular tone—</i>						
Good	..	..	..	18·6	28·2	48·7
Poor	..	..	..	28·8	12·1	5·8
Average	..	..	..	52·6	59·7	45·5
Anxiety state	..	..	..	57·7	66·0	63·5
Hysteria	..	..	..	25·	23·5	19·2
Psychopathic personality	..	..	..	9·6	9·3	14·1
Depressive state	..	..	..	20·5	19·2	23·1
Paranoid state	..	..	..	2·6	1·7	1·3
Obsessional state	..	..	..	1·3	1·0	1·3
Mental deficiency	..	..	..	·7	0	·7
Epilepsy	..	..	..	1·3	·6	1·3
Other mental disorders	..	..	..	·7	·3	0
Physical disease	..	..	..	2·6	2·6	5·8
<i>Intelligence.</i>						
<i>Progressive matrices—</i>						
Above average	..	..	..	24·2	30·8	31
Below average	..	..	..	36·2	29·0	25
<i>Vocabulary—</i>						
Above average	..	..	..	20·0	27·0	37
Below average	..	..	..	20·0	27·0	11

attitude and the surrender to feelings of inferiority had played an important role in the development of neurosis in the microsomatic group, although the Adlerian school would no doubt assume this to be the dominant factor. In fact, we find in all three groups considerable evidence of predisposition to neurosis.

Slater (1943) has clearly demonstrated that the tendency to develop neurosis under stress is directly related to the degree of neurotic constitution.

An assessment of the degree of neurotic constitution may be made from the following data which are, according to Slater (1943), its best indicators:—

1. Clinically abnormal personality.
2. Neurosis in childhood.
3. Positive family history.
4. Poor work record.
5. Repeated nervous breakdown.

TABLE VII.

	Microsomatics (156).	Mesosomatics (688).	Macrosomatics (156).
	%	%	%
<i>Clinically abnormal personality—</i>			
General instability	45.5	48.8	52.6
Weak and dependent	57.7	49.7	37.8
Anxious	60.1	62.9	50.6
Touchy and suspicious	29.5	31.1	33.9
Cyclothymic	29.5	31.6	28.9
Schizoid	26.3	33.3	31.4
Hysterical	21.2	24.3	21.2
Obsessional	22.4	24.7	22.4
Hypochondriacal	26.9	32.7	16.7
<i>Childhood neurosis</i>	44.2	39.7	37.2
<i>Positive family history</i>	87.2	88.6	87.8
<i>Poor work record</i>	10.25	6.7	7.1
<i>Repeated nervous breakdown</i>	5.8	6.4	5.1

Data on these factors are shown in Table VII, from which it will be seen that there is a high degree of neurotic constitution in all groups as shown by the high incidence of clinically abnormal personality, positive family history and childhood neurosis.

The percentage distribution of exogenous aetiological factors is shown in Table V, and no significant differences occur between the three groups. The effect of such exogenous factors, according to Slater (1943) is to determine the time and to some extent the intensity of the illness.

To summarise, we may say that there is evidence of considerable constitutional predisposition to neurosis in all groups and that a multiplicity of factors operated in the causation of the illness. The Adlerian concept of reaction to physical inferiority cannot therefore be given a dominant role in the aetiology of the microsomatic group but might have played a contributory part, together

with many other causative factors, both intrinsic and extrinsic as a result of whose interaction the illness developed.

In conclusion, it is interesting to note that the psychological correlates of body size are found to differ from those associated with body type. Whereas the extreme types of body size show significant differences in the incidence of personality attributes, the extremes of body type, the eurymorph and leptomorph, tend to be associated with hysterical and anxiety reactions respectively, which showed no significant differences in the types of body size.

SUMMARY.

1. The various physical attributes used as bases for study of relationships between physical and mental characteristics are summarised, and it is noted that little attention has been paid to the factor of body size as opposed to body type.

2. The factor of body size is described. Its universality and importance is indicated by its consistent elicitation in factorial and growth studies.

3. The theoretical considerations for constructing indices of body size are considered and it is considered inadvisable to use absolute measurements when coefficients of variation differ widely. An index consisting of the product of stature and transverse chest diameter expressed standard measure was used in the study.

4. The distribution of the body size index in a group of 1,000 soldiers is given and the group was arbitrarily divided at points of one standard deviation from mean into microsomatics, mesosomatics and macrosomatics according to body size.

5. The three groups so demarcated were compared statistically in incidence of personality and a large number of items relating to neurotic illness. Statistically significant differences were found between microsomatic and macrosomatic patients indicating a higher incidence of weak dependent timid and hypochondriacal traits of personality in the microsomatic group which was also inferior in musculature and intellectual level to the macrosplanchnic group. The macrosomatic group tended to be more active, aggressive and rebellious.

6. No significant relationships were found with clinical types of neurosis. This finding is of special interest as previous studies by the author have established relationships between physical type (as opposed to size) and diagnostic category; thus indicating different kinds of affinity between body type and body size with psychological attributes.

7. The possible role of body size in the aetiology of neurosis is considered with special reference to Adler's theory of physical inferiority. This factor is considered probably to play a minor role compared with constitutional, genetic and other exogenous factors.

8. Although the findings are of intrinsic interest and provide further evidence of complex relationships between physical and mental characteristics the degree of association is too low to be of diagnostic or prognostic value in clinical practice.

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THE ROLE AND FUTURE OF PSYCHOTHERAPY WITHIN PSYCHIATRY.*

By JOHN RICKMAN, M.D.

1. It may be well to begin by delimiting the term psychotherapy; to me it has two aspects:—

(a) It is a procedure of verbal interchange between patient and doctor in which the phenomena presented by the patient to the doctor during interview are interpreted by the doctor to the patient—to the end that the patient's mental pain shall be relieved (by the interpretation) and he shall have an increased understanding and mastery of the impulse-laden, unresolved, emotional conflicts in his own personal past experience, and a better insight into his own personality.

(b) Psychotherapy is also a procedure in which transference phenomena are manipulated by the doctor, whether or no he is conscious of the nature of those phenomena within the patient or in himself.

This double-channelled definition is positive, i.e., it states what happens, but it does not exclude the simultaneous or alternating use of non-psychotherapeutic procedures such as induced hypoglycaemia or narcosis or fits (which are sometimes given the lordly title of biological treatments). This definition also covers most of the procedures of Group Psychotherapy, which I shall discuss in more detail later.

2. It may also be well for a moment to discuss Psychiatry, within which it would seem psychotherapy has both a role and a future.

Psychiatry used to be a circumscribed area of medical activity into which one class of troublesome people were sent when their behaviour was conspicuously odd (prisons, to which the other class of troublesome people were sent, were for a time, strangely enough, reckoned outside the boundary of psychiatry). Now-a-days psychiatry is an area of activity which people actually seek to enter of their own accord, because they feel at odds with themselves and because they know that they can be helped to help themselves. Who would have guessed, say, 40 years ago, that insight would *increase* the demand for psychiatry?

These changes in the relation of psychiatry to the community and the demand for psychiatric help are due in such large measure to the influence of psychotherapy within and without the profession that one would almost suggest a title for another evening's discussion: "The Role and Future of Psychiatry without Psychotherapy."

3. If we enquire into the reasons which have given psychotherapy such influence I think it can be summed up quite simply: (a) psychotherapy has

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methods of research and therapy which can be taught, and the results of the psychotherapist's investigations can be brought within fairly generally understood frames of reference ; and (b) there is a sort of professional morale question involved—both the patient and the doctor invest in the same business and both therefore have an interest to make it a going concern. The patient risks his future happiness and a good deal of time and money in the therapy, the doctor invests a good deal of his time and his reputation. The extent to which this enterprise will continue to yield dividends depends on the extent to which both parties can learn to face unpleasant facts in the present. The most important feature of any psychiatric investigation is the influence of mental pain upon the course of human behaviour, and a study of the vigorous defence which is put up by patient and psychotherapist against the acceptance of the unpleasant has to be given a high priority in their joint undertaking.

4. It is a mistake to think that the founder of modern psychotherapy merely by action of intellectual genius hit upon a series of ideas useful in the relief of mental suffering. It is never thus in the progress of the human sciences. Each step has to be won at the cost of overcoming painful personal resistances, the dissolving away of carefully guarded defences involves an expenditure of effort in self-mastery ; progress in psychotherapy is not an intellectual achievement only, nor mainly, is it a morale issue—and like military morale in time of war it involves facing an enemy, this time an internal one—one's own disruptive and destructive impulses, and one has to keep on being on the watch for their influence on current behaviour. But psychotherapists are not the only people with a professional interest in the relief of mental pain, the clergy are much concerned with the pain of guilt. One of the reasons why the Church has not in the last thousand years or so added materially to our knowledge of mental pain lies in the fact that the clergy have not devised a technique for the investigation of mental pain, nor had psychiatry until recently.

5. The psychotherapist's work, like that of the scientist generally, is essentially a-historical. The data that bring conviction to him and to the patient are those memories and personal attitudes which arise in the immediate present, "the living present"—that four seconds of *now*—in the presence of the psychotherapist. Anamneses are events recalled, history-taking is a collection of data which by itself adds but little to the patient's experience of himself in his unpleasant, disruptive aspects. Self-knowledge does not come by recollection but by re-experiencing ; unless the recollection impinges on a personal relation in the present, and the interrelations of the memory and the current personal relationship are explored, mere recall does not make an almost irreversible effect upon the person concerned.

The technique of the psychotherapist consists in the management of the interview so that transference phenomena can appear with the least possible distortion to the end that the patient can match against one another the attitudes and ideas which emerge from the past and those that are seen to exist in the present—it is the example of the testing of reality as far as possible under controlled conditions. I call the analysis of free associations in the transference situation the "social instrument" of research and therapy. (Unfortunately, to learn the use of this "instrument" requires several years

of training.) The other "instrument" is that simple collection of rules for the elucidation of unconscious thought processes which Freud gave us in "The Interpretation of Dreams." By thorough and patient application of these two techniques to the minutiae of the patient's utterances and gestures the great advance in psychiatry has been made, the psychiatrist gains a new quality of interest in his material, and many patients have been given good grounds for believing that their condition was not incurable.

6. So far I have mentioned only the therapy of individuals taken one at a time. Group therapy is of two kinds: (a) a number of people are assembled together for purposes of explanation of their condition or for exhortation, or for that "companionate therapy" which comes when groups are formed mainly for the purpose of social amenity; (b) the other kind, to use the famous phrase of Dr. Bion, its originator, makes "the study of intra-group tension the task of the group," i.e., the members of the group study the group-cohesive and the group-disruptive forces operating within themselves as individuals and in the group. This latter kind of Group Therapy has that quality of a-historical research which characterises science and which in individual therapy has given us most of our ideas and data.

With any kind of psychotherapy, individual or group, there is one question it is most useful to ask oneself: what proportion of the time and energy during therapeutic sessions is given to the study of the defences against personal or group disruptiveness? According to the answer to this question the various kinds of therapy can be ranged in a sort of rank order; my guess is that those high in the scale furnish most to psychiatric research and give the more satisfactory therapeutic results, those low in the scale have a shifting population of adherents, are least keen about integrating their findings with that of other research workers, and the range of their therapeutic successes is less.

7. In speaking thus far of psychotherapy stress has been laid on pain, disruptiveness and similar disquiets of the mind. There is no such thing as "Psychiatry without Tears" and it is as well to face the fact. In good psychotherapy, however, an equal attention is given to joy and creativeness, but this aspect can never be treated in isolation from its opposite.

It would be a mistake to ignore the valuable by-products of psychotherapeutic work, namely, the insight gained into the structure of the personality; research on this matter, however, cannot be isolated from the general problems of the patient, no matter how clever or ambitious the research worker may be. In the human sciences pure research is usually a stultifying self-delusion, there is only operational research. If a research worker goes to a patient to get answers to his own questions he does not get far in the exploration of the underlying problems of human personality—his research can be left in the library, it is usually of but little use to the clinician. A thesis, however learned, however much it is stuffed with statistics, tells us but little about the woes of the suffering patient if it does not treat at first hand with anxiety, guilt and despair.

In the other kind of research—Operational Research—the patient (or a group) calls in the therapist and there is that mutual investment of energy to which I have already referred. In this case the patient's (or the group's) own

questions have top priority and the research worker's questions and curiosity have second place. In the field of the human sciences research and therapy are inseparable, for a patient cannot disclose the deeper levels of his mental pain unless he has the experience that the process of exploration gives relief to his pain. I believe this is true of groups too, though some group therapies seem to give more relief than they actually do; both kinds of therapy have to guard against the denial of painful problems and see that there is not an escape into temporary and unstable solutions.

8. Now as to the role of Psychotherapy within Psychiatry :—

(a) Its emphasis on the inseparable connection between research and therapy is a necessary reminder to psychiatry that it is quite as much dependent on the human sciences as on the physiological and other non-human biological ones.

(b) The genetic studies of the development and malformation of the personality, inevitable in any thorough-going psychotherapy, will help psychiatry to see more clearly the interrelation of individual development and the social cultural patterns in which that individual grows up.

(c) The free-association studies of the psychotherapist in the a-historical transference situation give to psychotherapy a research instrument which no other branch of psychiatry affords in anything like the same potency.

(d) The fact that the psychotherapist is compelled to face the most painful issues of human maladjustment without resort to evasion such as placebos, gives to psychiatry an almost automatic index of its own professional morale, since a repudiation of serious professional attempts to deal with serious clinical problems cannot be made without those thus exercising their indifference becoming somewhat conspicuous in a world of suffering humanity.

(e) Not least psychotherapy has proved successful in restoring to full capacity patients who were formerly incapacitated by neurotic disabilities that did not respond to other forms of therapy. Its role in this direction is extending, and these extensions of remedial power have raised not unwarrantable hopes in the patient population and made the practice of psychiatry more interesting to its practitioners.

9. As to the future of Psychotherapy within Psychiatry :—

(a) This depends on the freedom of locomotion given to the psychotherapist within the psychiatric field. Any move towards limiting psychotherapy to the neuroses is retrogressive. Both O.P. and I.P. facilities should be available to the psychotherapist even if for years he does not show much in the way of improvement in his cases.

(b) Even though the disposal and direction of the psychotherapist's time and energy are—or seem to be—dictated by the enormous number of cases calling for quick therapies, every psychotherapist should be free, and indeed, be encouraged, by the organisation he serves, to have at least one case on which he can spend an unlimited time. I can testify to the effect of such a permission on the raising of psychiatric morale, for during the war, on the advice of Brigadiers J. R. Rees and Sandiford, every Army psychiatrist in therapeutic work, no matter how vast his patient load, was allowed a case on which he could spend an hour a day for as long as the psychiatrist himself thought necessary.

I would go so far as to say that the future of psychiatry depends on such measures, which conserve the research and therapeutic impulses of the psychiatrist and give him some hope and a little scope.

(c) Since this is a section of social psychiatry (which is a relatively new idea) as well as of psychotherapy (which is half a century old—how time flies!) and since it is the inaugural meeting, I would like to add a word about the scope and possible future of social psychiatry based on experience of psychotherapy.

It is a field for operational research, not for quizzing by ambitious workers who want new worlds to conquer. The psychiatrist will have to earn his entry into this field by being able to serve its deeper needs. Research and therapy must go together here, and we must freely acknowledge that so far no one with the genius of Freud has arisen among us to give us even the most elementary advices for interpreting the data we are faced with; it is both imprudent for ourselves, unfair to psychiatry and grossly unfair to the public to lay claims we cannot amply fulfill.

The exercise of psychotherapy upon individuals teaches us, to say the least, the prudence of humility; the temptation to offer to humanity in its present distraught state more than we can give is one which we need to bear in mind. We do not know the remedies for the ills of our society because our notions about the aetiology are still so dim.

The technical methods of this new research and therapy may well be different from that we use with sick individuals, but the basic principles of the work will probably be much the same: to give priority to the client group's need and let the doctor's curiosity and therapeutic ambition come second, "difficulties" in the way of the research have to be considered as part of the field of therapy and research; the study of resistances and the careful painstaking overcoming of them will probably yield more research data to the doctor and more relief to the client group than any other method of approach. The way of individual psychotherapy has been hard enough, but though hard, rewarding; the way of social psychiatry will probably be even harder, let us hope it will be still more rewarding.

May I conclude with a passage from Walt Whitman which Churchill quoted on the radio in one of the dark days of the War:—

"Now understand me well, it is provided in the essence of things that from any fruition of success, no matter what, shall come forth something to make an even greater struggle necessary."

APPENDIX.

The paper to which this is an Appendix contains nothing new and, though perhaps suited to an Inaugural Meeting, would not be worth printing were it not for the fact, as the discussion following it showed, that its statements were generally misunderstood. An explanation—to be sure unusual in a paper that contains no original thought—may nevertheless be useful, and a personal note may perhaps be excused.

One of the striking things about the discussion, to me at any rate, was the fact that several members referring to this paper said it was all very well, *but*

they were not psychoanalysts, nor could they spend unlimited time on a single patient. This clearly indicated that the paper had misfired.

The crux of the matter lies in the psychiatrist's conception of the function of, and his role in, the psychiatric interview, that is to say, in the technique of management of the two-person relation which is created when a patient asks for help because of a psychiatric complaint. Fact-finding can be separated from therapy, but—such is the nature of the human mind—the *range* of the facts thus made available will be more limited than would be the case were therapy and fact-finding given a more equal priority. To say this is not to belittle the scientific value of research and deduction within the limited field, nor for that matter to deny the fact that the range of data is unlimited when therapy is given first place. The important thing is that mental pain benumbs the faculties (call it repression or resistance if you will), and the research worker, if he is wise, will reckon on the fact that the range of his data is restricted by factors of which his informant is unconscious and of which the researcher too may have just as active an aversion.

This by way of preface to the psychiatric interview—the best gift of psychiatry to medicine. To put it too briefly, the psychiatrist should first get clear in his mind and then disclose to the patient at the appropriate moment (timing is an art, fact arrangement a science) the relation between two sets of facts or sequences of facts. The one sequence is the chronological unfolding of the events of the patient's "history," so that both he himself and his doctor can get a picture of him as a person who has changed and developed in the course of time and through the impact of his impulses and environment. The physician is naturally tempted to complete this picture sequence as fully as possible in the time allotted to the interview, i.e., to get "the history of the person" as well as the history of the complaint. In the course of listening to the history, at the back of the physician's mind, there may be a most active sorting of data into categories, a veritable whirr of Hollerith, and the classifying frames of reference can be the most various and scientific. By long practice this sorting and matching process—particularly matching against the pattern of other case histories—can go on so smoothly that the machinery of the doctor's thinking goes unnoticed by his patient; when the thinking is smooth the doctor's intrusions and interrogations upon the patient's narrative is also usually smooth. But the physician, in the interest of research no less than of therapy, must give ear to another sequence, viz., the events occurring in the consulting room itself. This is the a-historical part of the investigation. When, on one occasion, a patient burst into a psychiatrist's consulting-room with the remark, "Doctor, my sister has played no part in my life," he was voicing not only a piece of history, albeit with a negative sign attached to it, but he was behaving in the a-historical present. He knew his doctor was "one of those Freudians" and he wanted to "clear away a lot of that nonsense" from the very beginning. This is a gross example, but it illustrates, perhaps almost to exaggeration, that the current interlocution is manipulated by the patient, and unless he himself is on the watch, the physician too tends to be manipulated in order that unconscious needs may be satisfied which, though dating from the past are also active in the present. The patient just referred to "gave the

game away," a fact which any psychiatrist could observe. But when the game is not given away, when the deflection of attention is unobtrusive, the physician must be on the alert for any deflections caused by the patient or himself.

A good psychiatric interview has something of the atmosphere of conversation among sensitive and well-mannered people, at least on the doctor's side. In polite society at least half of a person's attention is directed to the mood and the slight indications of a wish to change the subject on the part of the interlocutor, while the rest of the attention is given to the topic and to its pleasing development on a conscious rational plane. In the psychiatric interview the objectives (what Konstantin Stanislavsky called the super-objectives) lie outside the usual topics of conversation or customary thought; they concern the structure of the personality and the failures of its function. The patient always, and the physician too, unless he is on his guard, steers the conversation so that nothing shall arise which tends to threaten or disturb the structure and function of his personality, which is at best in a condition of quasi-stable equilibrium. The physician's duty is to discover and disclose the factors which threaten the equilibrium without upsetting it. The comparison between the psychiatric interview and conversation in polite society, though it is incorrect in respect to *aim*, has a certain usefulness when considered as a *technique* of perception of personal feeling and thought. If psychiatry is to give a lead to medicine in the matter of interviewing, I think it important that we should be clear that there is no question of an entirely new skill being employed, but that a skill (which is widely distributed in the population, particularly in the "interviewing professions," i.e., medicine, law and the Church) is in the case of the psychiatric interview developed to a far greater extent, and to a "depth" that is not only comparatively little employed, at least consciously, but is hardly dreamt of in professional circles outside of psychiatry with a psycho-dynamic orientation. Put briefly, we do not do things in or with our interviews which other people are incapable of doing, but we are guided by considerations which others, to their loss, tend to ignore. We on our side also endeavour to guide the course of the interview and are, of course, influenced by our theories of psycho-dynamics and personality development; but though we are so influenced we have, nevertheless, to give the patient such freedom of expression as to allow of spontaneity both to his utterance and to his underlying mood. This freedom is important because it allows data to appear which the physician is not looking for (thus, his theories can be checked and corrected), the patient feels that the dignity of his personality and individuality is being respected (a point of growing importance when medicine is becoming more and more a Department of State), and by the establishment of a two-way channel of communication the physician is given an opportunity to feel his way into his patient's capacity for (or the restriction of) social relationships.

The psychiatric interview can be—should be—a sampling technique for discovering the quality and flexibility of the patient's social relationships. The physician by the exercise of care and discernment (if he has an appreciation of psycho-dynamics) can uncover elements in the patient's past history of which he himself is and was unaware; I refer particularly to his conflict-ridden relation to parents and siblings. If the physician has trained himself to discern

the roles which the patient, all unwittingly, thrusts upon him in the course of the interview, he will when taking the history get some light on the patient's relation to people at critical periods of his life (critical periods, when conflicts are left unresolved—and being unresolved are carried over and unbalance the equilibrium of subsequent years—these are of special importance to psychiatric interviewing).

There are two sorts of facts in a psychiatric interview, those that the psychiatrist needs to know to make a diagnosis, and those he needs to know in order to get on with the treatment. When obtaining the former the psychiatrist's mind has to be predominantly and actively concerned with norms of behaviour, disease syndromes and neuro-psychiatric processes that have not yet been given a clear definition—he has, as it were, to feel his way into the body (or body mind if you will) of his patient. When obtaining the latter sort of facts that he will use in psychotherapy, the psychiatrist's mind has to be more passive and receptive and to be predominantly concerned with feeling his way into the social and emotional life of the patient. By social, I mean his relation to people as distinct from his psycho-physiological constitution and the vicissitudes of bodily maladjustment. The facts required in this category are mostly of a kind that cannot be obtained by question and answer, they emerge as a result of the social and therapeutic setting of the interview itself. The distinction between these two sorts of facts is arbitrary but may be useful as a rough indication of the kind of contribution that psychotherapy has given to psychiatric interview technique.

In the discussion at the meeting it seemed to me that some who took part assumed that because they were not psychoanalysts the principles outlined in the paper were not theirs to apply. If this is a legitimate inference the paper failed badly in its main purpose. Perhaps the difficulty lay in the meaning given to the words (§ 5) “the analysis of free associations in the transference situation” (the “social instrument” of research and therapy). I am aware that when this procedure is given the highest priority and is pushed to its limit the term psychoanalysis alone is justified. It may be remarked that the general principles can be applied in any degree of concentration and there are usually moments in most psychotherapeutic interviews when, if the psychotherapist is alert to the possibilities, these general notions can be used—to the enlightenment of the patient and the intellectual satisfaction of the physician.

When writing this paper I tried to keep in mind the title of the Symposium of which it was a part and to use only such concepts as were at the same time fundamental, in my view, to psychotherapy and common to all schools of thought. Freudians, Jungians, Adlerians and the inchoate host of eclectics may rebuke me that I have not said enough, but none of them I hope will reprove me for having said too much.

When it comes to that, what is all this business of psychotherapy about? The neurotic's trouble is a malfunctioning so persistent that the very structure of his personality seems to be affected by it—more boldly, we may perhaps say it *is* affected by it. The psychotherapist's task is to change the functioning so that the “set” of the patterns of behaviour shall be consistently more

flexible, i.e., adaptable and effective. (Effectiveness in this sense is not to be equated with extravert efficiency—though with people in the Western culture that may be frequent—but with a decrease in dammed-up tensions, blocked of outlet, with corresponding strain.) Here I wish to put in a personal opinion, but one that is shared wholeheartedly by many psychotherapists, and half-heartedly—perhaps because of the terrific implication—by many more. I cannot see how a maladjustment or constraint of personality that has persisted for years, and broken out conspicuously for the first time, maybe, in adult or adolescent life, can be readjusted except by the re-experiencing of the original conflict situation and thus working out a new and better solution.

"But surely," you may ask, "there are psychotherapies, and ones that are worthy of the name, which do not aim at or involve this re-experiencing and working through process? Hypnotism, for example, which does not necessarily employ the interpretative activity to which reference is made in the first paragraph? Are you going to deny to these therapeutic procedures the name of psychotherapy?"

Perhaps this fair and reasonable criticism was in the minds of the contributors to the discussion who said that they were not psychoanalysts. It touched on the major omission of the paper.*

What I have tried to conceptualise is the process of radical change in the structure and function of the personality, i.e., the attainment of a point of irreversibility in the process of change. The ameliorative procedures such as hypnosis, indeed, most of the "short term therapies" (how well named!) do not reach, or attempt to reach, that point of irreversibility; but they have claim, I admit, to the term psychotherapy.

So the lop-sidedness of my paper is apparent, but on the other hand I am loath to use two general names for psychotherapy. That a scale could be drawn—or several—is beyond doubt; the drawing up of such scales, with their correlates (see § 6) may even be useful, particularly if attention is paid to the causes of failure in effecting "irreversible change" in the procedures studied.

But to return to the general discussion. The title is too narrow; "The role and future of psychotherapy within *medicine*" would provide occasion for a useful link between general medicine and psychiatry because inevitably it would bring out in clear outline the technique of the psychiatric interview—that modern discovery of the dynamics of the doctor-patient relationship.

* The second, and minor, omission, was pointed out by Dr. Bierer in the discussion viz. that not *all* of psychotherapy is a verbal interchange. I should know that: in the course of an analysis of a very disturbed schizophrenic with depressive features the patient hid herself within her only garment, a blanket, so that only the eyebrow showed; nothing daunted I continued the conversation from where we left off last time and noted the changes in that eloquent but only visible member, which changes—a frown, scowl, surprise, a flicker of amusement, a softening of the curve—indicated the changes of her mood and thought. My surmises proved correct for when next she displayed her face and used her voice she corroborated the general trend of my guesses as to what had gone on in her mind. That session was no verbal *interchange*—it might even be called an "eye-brow" analysis—but there was an endeavour to verbalize, to conceptualize and make concrete "in the here and now" what was occurring concurrently in her mind.

RORSCHACH PATTERN IN DUODENAL ULCER.

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INTRODUCTION.

THIS study is part of an investigation into the physical and mental status of a small series of patients with duodenal ulcer undertaken at Guy's Hospital. Each patient in this series had a routine biophysical and biochemical investigation, a clinical interview and the Rorschach test. In addition, information about the patient was gained from other sources, such as his relatives and employer, and his behaviour while in hospital was kept under review. In a majority of the patients examined, phases of activity of the ulcer dyspepsia were correlated in time with crises in the patient's personal life. The Rorschach patterns from the records of these patients are presented here for comparison with those found in other disorders, and for the assessment of certain features common to this series.

In the Rorschach test, the stimulus material is relatively unstructured; the images which the patient produces in response to the test are in large measure a projection of his own mental content. The test is administered and scored, as far as possible, under standard conditions. The test result is thus an approach to an objective rating of personality, although complete objectivity, for many reasons, cannot be obtained. The chief value of the test in clinical practice lies in the capacity of the test material to evoke a certain sequence of reactions; from the configuration of these a skilled interpreter may derive a qualitative personality pattern. The value of the test is greatest when the record is taken as part of the body of clinical data, and interpreted with it. Although the aim of the test is to arrive at a qualitative assessment, some aspects of it can be expressed quantitatively; this study is confined to an appraisal of certain general features of the records and some of the quantitative relationships. For those acquainted with the Rorschach notation, a numerical summary of each record is given in the appendix.

MATERIAL.

Twenty consecutive cases of duodenal ulcer, admitted to the medical wards between November, 1947, and July, 1948. The reasons for admission to hospital were: in 14 cases, failure of the dyspepsia to respond to medical treatment; in four cases, haemorrhage from the ulcer; in two cases, associated or unrelated condition. The age range was 27-62; average 42. Half the patients were between 36 and 45.

The group in general is one of chronic duodenal ulcer; the duration of illness ranged from three months to 20 years; the average duration was 10 years. One patient (R.C.) presented a clinical picture different in kind from the remainder; the condition in his case could be termed an acute ulcer.

In all cases in the series, the diagnosis of duodenal ulcer seemed to be reasonably certain.

RESULTS.

The number of women in the series is too low to allow of any assessment of sex differences. The records of the four female patients did not differ grossly from those of the males.

1. *Personality type.*

Two records with marked obsessional features were found (C. B., W. P.) and two with marked hysterical features (J. E., W. W.). The remainder showed a wide range of personality features in varying combination. No predominance of any one type was found.

2. *Anxiety.*

In five cases (C. G., H. B., R. B., L. T., A. F.), the record was abnormally short, with rejection or failure to respond to some of the cards; as many as seven cards were rejected by one patient. This represents a failure to adapt to the test situation. In four of these cases (C. G., H. B., L. T., R. B.) the failure was an expression of marked anxiety; in one (A. F.), besides anxiety, there was an element of contempt for the test. Three other patients rejected one card each. In the normal person, rejection of cards rarely occurs. In this series, the cards most frequently rejected were Cards VI and X. Because of its fragmented pattern, Card X is not easy to integrate into a whole response (W.), and because of its bright colours, it presents a strong emotional stimulus. Card VI, as is well known, is especially disturbing to those in conflict over sexual relationships.

In three other records, the presence of moderate or marked anxiety was shown by the shading responses (K, k): S. J., F. R., C. C. It has to be recalled that in a group of patients of this kind, some degree of anxiety may well be due to the presence of a chronic painful illness which may threaten the patient's livelihood, as it did in these three men.

As an abnormally low productivity on the test may signify anxiety, so an abnormally high number of responses may represent a different reaction to the same internal state: compensatory over-activity as a reaction to internal unrest. An unusually high total of responses was found in two patients: C. B. (68) and F. P. (90). The latter would have given more, had he not been stopped on several cards.

3. *Emotional reactivity.*

The proportion of responses to the last three (coloured) cards gives some index of the subject's reaction to an emotional stimulus; if this proportion is less than 30 per cent., the subject may be said to show failure to respond

adequately to emotional stimulation, either from a particular psychic orientation ("introversion") or because he fears his emotional life and cannot handle it. Ten of these twenty patients gave less than 30 per cent. of their responses to the last three cards. Only one of these (A. F.) showed a tendency to introversion, as judged by an excess of movement over colour responses; in the other nine, there seemed to be a morbid limitation of emotional reaction.

The quality of this reaction may be estimated from the type of colour response: whether the reaction is under rational control (FC), or whether the subject is liable to be swept away by emotion and think or act impulsively (CF and C). Emotional liability (CF and C greater than FC) was found in eight patients.

4. *Signs of immaturity.*

An excess of animal movement responses (FM) over human (M) may be taken to mean either a failure to mature in spite of good potential capacity, or inability to mature owing to low intellectual level. No formal intelligence test was carried out on these patients; an approximate estimate of intelligence could be made from the clinical impression and from the vocational history. With one exception (R. C.) the level of intelligence was average or above. In nine of the patients, the ratio FM:M was greater than one. In one of these (S. R.) this may perhaps be interpreted as a regression, inasmuch as the patient was a man of 62, who had sustained a cerebral vascular accident, with concomitant reduction of his mental powers. In the other eight, its significance is that of a failure to develop, especially in inner reflective capacity.

In 12 patients, the proportion of responses with a content of animal form or movement (A) was more than 40 per cent. Animal responses are more common in children and dull adults; having regard to the general intellectual level of this group, this high proportion of animal responses may be regarded as pathological—a sign of immaturity, or of narrowing of the range of mental activity ("stereotypy").

The number of responses in which human figures were seen (H) was on the whole low. In card III, where human figures are almost universally seen by normal subjects, seven of the patients did not produce a human response. The poverty of such responses can be interpreted as a sign of failure to achieve satisfactory relationships with other people.

SUMMARY.

The Rorschach records of 20 patients with duodenal ulcer are reviewed. No predominance of a single personality type was found; the most conspicuous abnormal features were anxiety, emotional liability and immaturity.

APPENDIX.

Seven of these patients were tested by one of us (A. K.): 14-20; and the other 13 by O'N.: 1-13. The system of scoring was agreed upon so as to avoid discrepancies, and to render the two sets of records comparable.

1. F. M., male, 58.

Location.		Determinants.				Main categories of content.			
W	11	F	13	Fc	2	Total T	25	H	1
WX	3	M	2	FC	3	Total R.	25	(H)	3
D	9	FM	1	CF	1	W : M	11 : 2	Hd	1
d	1	k	1	C	1	M : sum C	2 : 4	A	8
S	1	Fk	1			(FM, m) (Fc, c, C')	1 : 2	Anat	5
						Popular	2	Obj	3
						Original			
						Per cent. last 3	25		
						A per cent.	32		
						Rej.			

2. H. K., male, 42.

W	8	F	23	Fc	1	Total T	25	H	4
WX	2	M	3	FC	1	Total R	36	Hd	2
D	22	FM	1	CF	1	W : M	8 : 3	A	11
d	4	m	1	C	3	M : sum C	3 : 6	Ad	3
		k	1			(FM, m) (Fc, c, C')	2 : 1	Anat	3
		Fk	1			Popular	5	Obj	7
						Original		Bot	3
						Per cent. last 3	37		
						A per cent.	40		
						Rej.			

3. H. J., female, 43.

W	7	F	9	Fc	2	Total T	25	H	2
WX	3	FM	3	C'	1	Total R	24	A	11
D	12	M	1	FC	3	W : M	7 : 1	Ad	2
d	1	FK	1	CF	3	M : sum C	1 : 4½	Anat	1
S	1	FK	1			(FM, m) (Fc, c, C')	3 : 3	Obj	1
						Popular	4	Bot	4
						Original	1		
						Per cent. last 3	37		
						A per cent.	54		
						Rej.	1 (VI)		

4. S. J., male, 33.

W	9	F	6	Fc	3	Total T	22	Hd	1
WX	5	M	—	C'	1	Total R	17	A	7
D	2	FM	1	CF	1	W : M	9 : 0	Ad	3
d	1	K	2	C	1	M : sum C	0 : 2½	Anat	2
		Fk	2			(FM, m) (Fc, c, C')	1 : 4		
						Popular	4		
						Original			
						Per cent. last 3	18		
						A per cent.	59		
						Rej.	1 (X)		

5. C. G., male, 27.

Location.	Determinants.				Main categories of content.		
W	1	F	3	Total T	13	A	2
WX	1			Total R	3	Anat	1
D	1			W : M			
				M : sum C			
				(FM, m) (Fc, c, C')			
				Popular	3		
				Original			
				Per cent. last	3		
				A per cent.			
				Rej. 7.	(II. III. IV. VI. VII. IX. X)		

6. R. C., male, 39.

W	2	F	21	FC	1	Total T	13	(H)	1
WX	4	M	—	C	2	Total R	26	Hd	1
D	15	K	1			W : M	2 : 0	A	8
d	5	k	1			M : sum C	0 : 3½	Ad	1
						(FM, m) (Fc, c, C')		Anat	1
						Popular	1	Bot	4
						Original		Obj	2
						Per cent. last	3 40		
						A per cent.	35		
						Rej.			

7. C. B., male, 43.

W	3	F	51	C'	1	Total T	50	H	17
WX	3	FM	3			Total R	68	(H)	2
D	22	M	10			W : M	3 : 10	Hd	20
d	24	m	1			M : sum C	10 : 0	A	14
dd	16	k	2			(FM, m) (Fc, c, C')	4 : 1	Ad	5
						Popular	5	Obj	6
						Original			
						Per cent. last	3 50		
						A per cent.	28		
						Rej.			

8. J. B., male, 42.

W	15	F	21	Fc	4	Total T	42	H	2
WX	3	M	1	C'	1	Total R	39	Hd	1
D	17	FK	2	FC	2	W : M	15 : 1	A	9
d	2	Fk	1	CF	4	M : sum C	1 : 9½	Ad	1
S	2			C	2	(FM, m) (Fc, c, C')		Obj	5
				Cm	1	Popular	3		
						Original			
						Per cent. last	3 25		
						A per cent.	25		
						Rej.			

9. H. B., male, 47.

Location.		Determinants.		Main categories of content.	
		Total T 21		A	7
W	1	F	5	Ad	1
D	8	FC	3	Ld	1
		W: M			
		M: sum C 0: 1½			
		(Fm, M) (Fc, c, C')			
		Popular 2			
		Original			
		Per cent. last 3 20			
		A per cent. 90			
		Rej. 5. (V. VI. VII. IX. X)			

10. L. T., female, 50.

W	1	F	8	C	1	Total T	19	H	1
D	8	M	1			Total R	11	Hd	2
d	2	k	1			W: M		A	1
						M: sum C 1: 1½		Ad	5
						(FM, m) (Fc, c, C')		Anat	1
						Popular 1			
						Original			
						Per cent. last 3 10			
						A per cent. 55			
						Rej. 3. (VII. VIII. IX)			

11. R. B., female, 30.

D	3	F	9			Total T	35	Hd	5
d	6					Total R	9	Anat	4
						W: M			
						M: sum C			
						(FM, m) (Fc, c, C')			
						Popular			
						Original			
						Per cent. last 3 45			
						A per cent.			
						Rej. 4. (III. V. VI. X)			

12. F. P., male, 43.

W	23	F	47	Fc	7	Total T	45	H	10
'AX	7	m	1	C'	5	Total R	90*	(H)	4
D	34	FM	5	FC	7	W: M	23: 9	Hd	6
d	20	M	9	CF	6	M: sum C	9: 11	A	20
S	6	FK	1	Cm	1	(FM, m) (Fc, c, C')	6: 12	Ad	9
						Popular	7	Anat	2
						Original	5	Obj	22
						Per cent. last 3 30*			
						A per cent. 32			
						Rej.			

* This patient was stopped after 10 responses on several cards.

13. F. R., male, 33.

Location.		Determinants.				of content.			
W	17	F	16	Fc	2	Total T	22	H	5
WX	4	FM	4	C'	4	Total R	46	(H)	3
D	21	M	6	FC	6	W : M	17 : 6	A	17
d	4	K	1			M : sum C	6 : 3	Ad	5
		k	2			(FM, m) (Fc. c., C')	5 : 6	Map	4
		Fk	2			Popular	6	Obj	4
		Fm	1			Original			
		kF	1			Per cent. last	3 31		
		KF	1			A per cent.	48		
						Rej.			

14. A. C., male, 38.

W	8	F	4	Fc	1	Total T	14	H	4
WX	4	FM	4	C'	1	Total R	18	A	5
D	6	M	3	FC	1	W : M	8 : 3	Ad	1
		K	1	CF	1	M : sum C	3 : 1½	Ld	2
		Fk	2			(FM, m) (Fc, c, C')	4 : 2		
						Popular	5		
						Original	1		
						Per cent. last	3 44		
						A per cent.	36		
						Rej.			

15. C. C., male, 29.

W	8	F	11	Fc	1	Total T	7	H	1
WX	2	FM	5	CF	3	Total R	31	A	11
D	21	M	1	C	3	W : M	8 : 1	Ad	4
		K	2			M : sum C	1 : 7½	Anat	2
		FK	1			(FM, m) (Fc, c, C')	6 : 1	Cloud	2
		Fm	1			Popular	5		
		Fk	2			Original			
		KF	1			Per cent. last	3 19		
						A per cent.	48		
						Rej.			

16. J. E., Female, 37.

W	5	F	9	Fc	2	Total T	19	Hd	2
WX	2	FM	5	c	1	Total R	24	A	6
D	13	Fm	1	FC	1	W : M		Ad	3
d	3	FK	1	CF	2	M : sum C	0 : 4	Obj	4
S	1	Fk	1	C	1	(FM, m) (Fc, c, C')	6 : 3		
						Popular	5		
						Original			
						Per cent. last	3 29		
						A per cent.	38		
						Rej.			

17. W. W., male, 45.

Location.		Determinants.				Main categories of content.			
W	6	F	5	Fc	2	Total T	14	H	1
WX	3	mF	1	FC	3	Total R	25	Hd	2
D	14	Fm	1	CF	1	W : M	6 : 2	A	6
dd	1	FM	5	C	2	M : sum C	2 : 5½	Ad	2
S	1	M	2			(FM, m) (Fc, c, C')	7 : 2	Obj	2
		Fk	2			Popular	5		
		KF	1			Original			
						Per cent. last	3 15		
						A per cent.	32		
						Rej.			

18. S.R. male, 62.

W	3	F	2	CF	2	Total T	21	H	1
WX	2	Fm	1	C	1	Total R	11	A	1
D	5	FM	4			W : M	3 : 1	Obj	2
S	1	M	1			M : sum C	1 : 3½	Bot	3
						(FM, m) (Fc, c, C')			
						Popular	4		
						Original	1		
						Per cent. last	3 36		
						A per cent.	45		
						Rej.			

19. A. F., male, 39.

W	2	F	2			Total T	7	H	1
WX	2	FM	2			Total R	5	A	4
D	1	M	1			W : M	2 : 1		
						M : sum C	1 : 0		
						(FM, m) (Fc, c, C')			
						Popular	3		
						Original			
						Per cent. last	3 20		
						A per cent.	80		
						Rej.	5. (II. IV. VI. IX. X)		

20. E. C., male, 49.

W	4	F	6	Fc	2	Total T	21	(H)	2
WX	6	FM	3	CF	4	Total R	17	Hd	1
D	6	M	1			W : M	4 : 1	A	7
S	1	Fk	1			M : sum C	1 : 4	Obj	3
						(FM, m) (Fc, c, C')	3 : 2		
						Popular	6		
						Original			
						Per cent. last	3 29		
						A per cent.	41		
						Rej.	1. (VII)		

SUMMARY OF MAIN FEATURES.

Rejections.—Eight patients rejected cards ; the number rejected varied from one to seven. There were no rejections of Card I ; four patients rejected Card VII, and four Card IX ; five rejected Card VI, and five Card X.

Responses to last three cards.—(Case F. P. excluded.) Only six patients are within the range 30-40 per cent. Ten are below this range, and three above. Considerable discrepancy is often shown between the M : sum C ratio and the proportion of responses to the last three cards ; the patients are sensitive to emotional stimulation but are unable to handle their reactions to it.

Variety.—In general, fair or good.

Fc responses.—Present in 12 cases, up to four responses.

FC responses.—Present in 11 cases, up to three responses.

CF responses.—Present in 12 cases.

C responses.—Present in 10 cases.

H and Hd responses.—Two patients saw no H at all, three saw only Hd. Seven patients did not see the human figures on Card III ; 13 did not see them on Card VII.

TUBERCULOSIS IN A MENTAL HOSPITAL. FIVE YEARS' MASS RADIOGRAPHY.

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In a previous paper (Early, 1946) I reported and commented on the preliminary mass radiography survey in the Bristol Mental Hospital in December, 1944. Each year since then the entire patient population has been subjected to mass radiography and in this paper the results of this work will be reported.

The procedure involved in subsequent years was considerably less cumbersome than in 1944, in that the Bristol Mass Radiography Department now has a mobile unit which visited the hospital, with consequent saving of time and expense. This fact explains why the total number of patients is slightly less in 1945 and 1946 than in 1944, the 1944 figures including the "floating population" in the hospital during the two months necessary to complete the survey. The subsequent surveys took about ten days to complete. The rising figure from 1945 to 1947 is an indication of the increase in overcrowding. The big increase in the 1948 figure is due to the fact that Barrow Hospital has been reopened, having been occupied by the Navy during the war.

To facilitate comparison the same method of classification will be used as previously. In reporting the 1947 and 1948 surveys it is considered unnecessary to include all the patients who were picked up in the original mass radiography and who have been regarded as inactive over a period of three years. Under the heading of "Inactive Tubercle (under observation)" will be included all patients who at one time have been considered active but have shown no radiological change over a period of three years, and all those who showed more than minimal infiltration although they never have shown any change in the X-ray or abnormal clinical tests to indicate activity. Included under "Total number examined radiologically" are those patients previously diagnosed or under observation who are followed up regularly on large films. Those not examined radiologically but showing no clinical signs of tubercle are regarded as non-tuberculous and the percentages worked out in relation to the total population. Included in the figures are patients who developed tuberculosis during the year and died during the same year.

RESULTS OF SURVEYS.

TABLE I.—*Mass Radiography Survey, 1944.*

Preliminary survey. 1944.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
Patients in hospital . . .	540	—	700	—	1240	—
„ X-rayed . . .	540	100	676	96.6	1216	98.1
„ not X-rayed—	—	—	24	3.4	24	1.9
Evidence of tubercle—all stages . . .	46	8.5	27	3.9	73	5.9
Active tubercle. . .	13	2.4	4	0.6	17	1.4
1. Minimal . . .	1	0.2	—	—	1	0.08
2. Moderately advanced . . .	2	0.4	—	—	2	0.2
3. Far advanced . . .	10	1.9	4	0.6	14	1.1
Inactive tubercle. . .	33	6.1	23	3.3	56	4.5
1. Minimal . . .	24	4.4	17	2.4	41	3.3
2. Moderately advanced . . .	9	1.7	6	0.9	15	1.2
3. Far advanced . . .	—	—	—	—	—	—
Pleural involvement . . .	3	0.6	—	—	3	0.2

1945 :

There were 1,209 patients in the hospital at the time of the survey (512 M., 697 F.), of whom 1,187, or 98.2 per cent, were radiologically examined (509 M., 99.4 per cent., and 678 F., 97.3 per cent.). Of these, 38, or 3.1 per cent. showed evidence of active phthisis (29 M., 5.7 per cent., and 9 F., 1.3 per cent.). There were 12 new cases amongst hospital “residents,” 10 amongst male patients and 2 amongst the female patients; 3 new cases were new admissions; 8 patients previously considered inactive (4 M. and 4 F.) were now considered active; 4 male patients previously considered active were now graded as inactive; 5 male patients known to be suffering from phthisis died during the year, and 6 patients graded as inactive (2 M., 4 F.) died of other causes. In addition, 2 patients died of miliary tuberculosis and another developed tuberculous broncho-pneumonia, from which he died. None of these had previous radiological evidence of infection. Three male patients showed evidence of pleural involvement; 2 had a pleural effusion.

TABLE II.—*Radiographic Survey, 1945.*

1945.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
Patients in hospital . . .	512	—	697	—	1209	—
„ X-rayed . . .	509	99.4	678	97.3	1187	98.2
„ not X-rayed . . .	3	0.6	19	2.7	22	1.8
Evidence of tubercle—all stages . . .	62	12.1	22	3.2	84	6.9
Active tubercle . . .	29	5.7	9	1.3	38	3.1
1. Minimal . . .	9	1.8	4	0.6	13	1.1
2. Moderately advanced . . .	8	1.6	3	0.4	11	0.9
3. Far advanced . . .	12	2.3	2	0.3	14	1.2
Inactive tubercle . . .	33	6.4	13	1.9	46	3.8
1. Minimal . . .	22	4.3	9	1.3	31	2.6
2. Moderately advanced . . .	9	1.8	4	0.6	13	1.1
3. Far advanced . . .	2	0.4	—	—	2	0.2
Pleural involvement . . .	3	0.6	—	—	3	0.2

1946 :

The population had risen to 1,238 (528 M., 710 F.) ; 1,212 (97.9 per cent.) of them were examined radiologically (520 M., 98.5 per cent., and 692 F., 97.5 per cent.) ; 20 M. (3.8 per cent.) and 11 F. (1.5 per cent.) showed evidence of active tubercle, i.e. 31 patients, or 2.5 per cent. of the hospital population. There were 5 new patients amongst hospital residents, 1 M. and 4 F. ; 1 new female case was a new admission ; 1 male previously considered inactive was now considered active ; 8 cases previously considered active (6 M. and 2 F.) were regraded to the inactive category ; 6 cases (5 M., 1 F.) of recognized tubercle died of the disease during the year. One female patient developed broncho-pneumonia following pleurisy and died ; 2 male patients previously not considered as tubercle developed the disease and died from it ; 1 male with active tubercle recovered mentally, resigned from hospital and was discharged. Four cases regarded as inactive (3 M., 1 F.) died of other causes ; 2 male cases showed pleural involvement ; 1 previously reported was considered non-tuberculous.

TABLE III.—*Radiographic Survey, 1946.*

1946.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
Patients in hospital . . .	528	—	710	—	1238	—
„ X-rayed . . .	520	98.5	692	97.5	1212	97.9
„ not X-rayed . . .	8	1.5	18	2.5	26	2.1
Evidence of tubercle—all stages . . .	53	10.0	25	3.5	78	6.3
Active tubercle . . .	20	3.8	11	1.5	31	2.5
1. Minimal . . .	7	1.3	6	0.8	13	1.1
2. Moderately advanced . . .	8	1.5	3	0.4	11	0.9
3. Far advanced . . .	5	0.9	2	0.3	7	0.6
Inactive tubercle . . .	33	6.3	14	2.0	47	3.7
1. Minimal . . .	23	4.4	12	1.8	35	2.8
2. Moderately advanced . . .	7	1.3	2	0.3	9	0.7
3. Far advanced . . .	3	0.6	—	—	3	0.2
Pleural involvement . . .	2	0.4	—	—	2	0.2

1947 :

The hospital population had still further risen to 1,274 (530 M. and 744 F.) ; 1,249, or 98 per cent., were examined radiologically (526 M., 99.2 per cent., and 723 F., 97 per cent.) ; 33, or 2.6 per cent. of the total population, showed evidence of active phthisis (21 M., 4 per cent., and 12 F., 1.6 per cent.) ; 4 new cases were discovered amongst the residents (3 M., 1 F.) ; 10 cases of new disease were amongst new admissions (6 M., 4 F.) ; 4 male cases graded inactive were now considered active ; 6 cases (5 M., 1 F.) previously considered active were now graded as inactive, having shown no radiological change over a period of three years ; 3 active cases (2 M., 1 F.) died during the year of tuberculosis ; 2 inactive cases (1 M., 1 F.) died or was discharged. Pleural involvement was evident in 2 patients, as last year ; 3 female patients previously under observation were now considered to be non-tuberculous.

TABLE IV.—*Radiographic Survey, 1947.*

1947.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
Patients in hospital . . .	530	—	744	—	1274	—
" X-rayed . . .	526	99·2	723	97·0	1249	98·0
" not X-rayed . . .	4	0·8	21	3·0	25	2·0
Active tubercle . . .	21	4·0	12	1·6	33	2·6
1. Minimal . . .	8	1·5	3	0·4	11	0·9
2. Moderately advanced . . .	8	1·5	6	0·8	14	1·1
3. Far advanced . . .	5	0·9	3	0·4	8	0·6
Inactive tubercle (under observation) . . .	20	3·8	7	0·9	27	2·1
Pleural involvement . . .	2	0·4	—	—	2	0·2

1948 :

The hospital population had been swollen to 1,415 by the opening of Barrow Hospital (597 M., 818 F.) ; 1,383, or 97·7 per cent. were examined radiologically. Evidence of active tubercle was present in 40 patients (2·8 per cent.) (26 M., 4·4 per cent., and 14 F., 1·7 per cent.). There were 4 new cases discovered amongst the hospital population, 2 M. and 2 F. There were 7 new cases amongst new admissions, 6 M. and 1 F. ; 5 cases considered inactive were now graded as active, 4 M. and 1 F., and 5 patients, 4 M. and 1 F., previously under treatment for active phthisis were transferred to the " Inactive " category. 5 patients, 4 M., 1 F., died from tubercle during the year, and 1 case of active phthisis died from other causes. One female patient with active phthisis was discharged during the year.

TABLE V.—*Radiographic Survey, 1948.*

1948.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
Patients in hospital . . .	597	—	818	—	1415	—
" X-rayed . . .	592	99·2	791	96·7	1383	97·7
" not X-rayed . . .	5	0·8	27	3·3	32	2·3
Active tubercle . . .	26	4·4	14	1·7	40	2·8
1. Minimal . . .	9	1·5	6	0·7	15	1·1
2. Moderately advanced . . .	8	1·3	5	0·6	13	0·9
3. Far advanced . . .	9	1·5	3	0·4	12	0·8
Inactive tubercle (under observation) . . .	24	4·0	11	1·3	35	2·5
Pleural involvement . . .	1	0·2	—	—	1	0·1

DISCUSSION.

The increase of disease amongst hospital residents in 1945 may represent a late occurrence of the war-time increase in tuberculosis reported in the M.R.C. Report on tubercle in war-time, 1942. The factors incriminated such as overcrowding and war-time dietary have not appreciably improved. The black-out does not apply but the ventilation of old grossly overcrowded buildings

is unsatisfactory. Five of the male patients, newly discovered, and 3 of those showing signs of activity previously considered inactive came from the same ward as did the male case in 1946, 2 male cases in 1947 and 1 male in 1948. This ward contains 112 patients and provides accommodation for deteriorated chronic psychotics. In such conditions of overcrowding, diet cannot be adequately supervised and ventilation is unsatisfactory. The number of beds available for the treatment and observation of tuberculosis is inadequate and unsatisfactorily situated; it is not possible to set aside complete wards for this purpose. Hence, patients considered inactive and falling into the mental category served by this large ward were transferred back there into precisely the same conditions as those in which they fell ill. We consider that rather than distribute cases considered inactive to such large units, they should be kept under supervision to prevent relapse. In order to keep these patients under better supervision, we have had to make use of our infirmary ward and to move this ward elsewhere, a solution which has further complicated the bed problem.

The total admissions in the B.M.H., which was 448 in 1945, rose to 588 in 1946, to 659 in 1947 and to 1,002 in 1948. It continues to rise. The tuberculosis question, therefore, increases in importance as a psychiatric and public health problem.

The number of new cases brought to light in the 1945 Survey, and the number of patients who died of tubercle not evident at mass radiography should place one on one's guard against neglecting other methods of diagnosis. Whether the "new" tubercle developed during the year or not, mass radiography represents an invaluable aid in diagnosis. Its limitations are recognized by its advocates; it should not lull one into a sense of false security. The 1947 miniature films of the patients newly reported, were all reviewed, and in one film it was possible in the light of subsequent pictures to say that there was a small lesion. Other routine methods of diagnosis have also been utilized—stethoscopic examination, 3-monthly weight charts, B.S.R., pulse, temperature, respiration and examination of the lungs on large films after all illnesses referable to the chest. Routine X-ray of all new admissions, which has been adopted since May, 1947, is a most important adjunct to early diagnosis and control. This is not possible unless there is an X-ray department in the hospital.

Criteria of activity have offered the same difficulties as heretofore. After initial discovery of radiological lesions, physical examination, sputum, B.S.R. and other clinical signs may help. Serial X-rays, however, are the most valuable guide. As an index of inactivity we have adopted the absence of radiological change over a period of at least two years, and preferably three years.

INCIDENCE.

Amongst male patients the incidence of active disease remains consistently higher than amongst females. This fact was commented on in my previous paper. Alstrom, Gentz and Lindblom (1949) have reported similarly.

TABLE VI.—*Incidence from Year to Year Compared to Two Recently Published Surveys.*

Active pulmonary tubercle.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
Bristol Mental Hospital :						
1944 . . .	13	2.4	4	0.6	17	1.4
1945 . . .	29	5.7	9	1.3	38	3.1
1946 . . .	20	3.8	11	1.5	31	2.5
1947 . . .	21	4.0	12	1.6	33	2.6
1948 . . .	26	4.4	14	1.7	40	2.8
Alstrom, Gentz and Lind-						
blom (1949) . . .	50	6.0	38	4.6	88	5.3
Lambiotte, Washington and						
Bozalis (1949) . . .	100	5.6 to	..	..	..	5.6 to
		6.2				6.2

Alstrom *et al.* (1949) quote Blomquist (1936) whose figures in the Lellhagen Hospital in Goteburg were 9.25 per cent. of 919 long-stay patients and 4.99 per cent. of 941 patients recently hospitalized ; and Malmros and Wessel (1937) in the Saint-Lars Hospital in Lund 5.8 per cent. active disease amongst 1,060 patients.

INCIDENCE AMONGST NEW ADMISSIONS.

The incidence of active pulmonary tuberculosis amongst new admissions in 1945 and 1946 was appreciable in spite of inadequate methods of diagnosis. It is interesting that the figures should be higher during 1947 and 1948, when routine films of all admissions were taken. The admission rate during these years had risen greatly.

TABLE VII.—*New Cases Diagnosed Amongst New Admissions.*

Year.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
1945 . . .	2	1.0	1	0.4	3	0.7
1946 . . .	..	..	1	0.3	1	0.2
1947 . . .	6	2.3	4	1.5	10	1.5
1948 . . .	6	1.4	1	0.2	7	0.7

INCIDENCE AMONGST "RESIDENT" HOSPITAL POPULATION.

The incidence amongst hospital "residents" has shown a yearly decline.

TABLE VIII.—*New Cases Amongst Hospital Population.*

Year.	Males.		Females.		Total.	
	Number.	%.	Number.	%.	Number.	%.
1945 . . .	10	1.9	2	0.3	12	1.0
1946 . . .	1	0.2	4	0.6	5	0.4
1947 . . .	3	0.6	1	0.1	4	0.3
1948 . . .	2	0.3	2	0.2	4	0.3

Relation of length of hospitalization to tuberculosis has not been tabulated. Routine radiological examination of chest on admission will give a better source of the required information. There is no doubt that a considerable number develop tubercle in hospital.

Comparison between the number of new cases occurring amongst new admissions and new cases diagnosed amongst hospital residents (Table VII and Table VIII) is valid for the year 1948, the only complete year where routine admission films were taken. This year's figures and those of 1947 tend to agree with the findings of Blalock and Funkhouser (1943), that the incidence of tubercle amongst consecutive admissions is greater than in the preliminary survey.

Recently Alstrom, Gentz and Lindblom (1949) have reported that tubercle is more frequent amongst patients who have been hospitalized for a long time—3·1 per cent. of schizophrenics in the 0-5 year group and over 7 per cent. of those in hospital over 5 years. They assume from this that the incidence is higher amongst the hospital population than amongst new admissions. Lambiotte, Washington and Bozalis (1949) maintain that the majority of patients probably contract the infection as well as the disease after their admission. Neither of these groups of workers has reported routine radiological examination of admissions coupled with careful methods of control.

Mortality—expressed as a percentage of the total deaths in hospital.

TABLE IX.—*Tuberculosis Mortality Rate.*

Average for 3 pre-war years.	Average for first 5 years of war.	1944.	1945	1946.	1947.	1948.
11·6%	10%	8·9%	8·7%	7·0%	3·1%	6·0%

The comparable figure for mental hospitals in England and Wales in 1948 was 7·5 per cent (Board of Control Annual Report to the Lord Chancellor, 1948).

It is significant how the tuberculosis death rate has fallen, even with a falling death rate in the hospital. Two of the 3 cases who died of the disease during 1947 imported their disease into hospital and died of it during the year, as did 3 of the 5 patients who died in 1948. In this last year the total number of deaths in hospital was the lowest on record, so that the figure of 6 per cent. gives an exaggerated impression of the number who died of the disease. Only one hospital resident died of tubercle in 1947 and two in 1948.

The classification of patients according to their mental illnesses has not again been attempted. Alstrom (1942) has confirmed that tuberculosis mortality is equal amongst schizophrenics and non-schizophrenics.

TREATMENT.

Under prevailing accommodation conditions it has not been possible to treat patients on strictly sanatorium lines. We agree with Lambiotte *et al.* (1949) that most patients are amenable to active measures of treatment and

we have not had to stop such treatment because of mental reasons. We have found that with early diagnosis, conservative rather than active treatment is usually indicated. The question of fitness for active physical psychiatric treatment, such as E.C.T., must always depend on the urgency of the psychiatric picture. Definitely inactive tubercle can be treated with these measures with fair safety. Active pulmonary cases should not be so treated unless the psychiatric picture is urgent and there are definite indications that the patient will benefit by such treatment. Curare is probably indicated in these cases.

The most urgent matter at present is that of accommodation. This remains unsatisfactory. In a previous paper I considered that the difficulties in regionalizing Mental Hospital Tuberculosis Services were too great to warrant discussion. Although building has become no easier, the regionalizing of the hospital services has made such a solution feasible. We consider that this is the only way in which the problem can be satisfactorily dealt with. If tackled piecemeal each hospital can at best provide a moderate service. Buildings at present available are almost invariably unsuitable and the cost of building separate units in each hospital or of converting available accommodation will be greater than the building of a new, up-to-date modern sanatorium which takes into consideration the especial needs of psychiatric cases. We would propose separate bed-space for the more disturbed type of case, both for treatment and convalescence, with separate living, eating and occupation therapy arrangements for these patients. The problem of the number of beds which should be available is difficult. Hamilton and Kidner (1925) consider that not less than 5 per cent. of the total mental hospital beds should be available for the treatment of tuberculosis. Klopp (1927) places the proportion at about 5 per cent. We consider that the number of sanatorium beds available should be in the region of 2.5 per cent. of the total hospital population and should be planned in the ratio of 2 males to 1 female. The optimum size should be about 150 patients and medical, nursing, radiological and accessory services should be of the highest standard. The Visiting Chest Consultant should have a knowledge of the special problems involved in mental hospital practice. Arrangements for the training of suitable personnel at sanatoria could easily be arranged.

Leonidoff (1938) disagrees with this method of dealing with the problem because of the tendency that there would be to send every suspected or arrested case to the unit with resultant overcrowding without accomplishing its purpose. He also mentions the factor of distance, which is a less valid reason with us than in the Hudson River State Hospital. Admission and discharge would, of course, have to be carefully controlled, but with a well-organized service this should not be impossible.

Klopp (1927) and Wicks (1940) agree with the policy of centralization. The latter author says that those in charge of the hospital at Brampton "are convinced that centralization of such treatment facilities (incorporating sanatorium and mental hospital features) offers the only satisfactory solution to the problem."

Without such a central tuberculosis mental hospital in the northern half of the south-western region of England alone small units would be required

at each of the five hospitals in the region. In England and Wales 99 such units would be necessary. It is unlikely that each would be adequately staffed and equipped.

STAFF.

Yearly mass radiography facilities have been available to all the hospital staff—100 per cent. of the nursing staff have consistently presented themselves for examination. Nurses on wards accommodating tuberculous patients have been encouraged to present themselves for X-ray 3-monthly. In 1945 one physician and one female nurse developed tubercle; in 1946 one male nurse and in 1947 one male and one female nurse. In a Memorandum on the Supervision of Nurses' Health (1945) it is pointed out that nurses in general hospitals are not so well safeguarded against risk of infection as are nurses working in sanatoria. This applies equally to nurses in mental hospitals. A central mental hospital sanatorium with staff trained in sanatorium practice offers the best safeguard to nurses. The financial privileges offered to nurses in charge of tuberculous patients should then be payable. The value of the proposed scheme for B.C.G. Inoculation of Hospital Nurses (1949) remains to be proven.

SUMMARY.

1. The results of five annual mass radiography surveys are reported.
2. The high incidence amongst new admissions has been commented on.
3. A fall in hospital mortality from tuberculosis is noted.
4. The question of the advisability of centralizing mental hospital tuberculosis services is discussed.
5. A brief note and comment on tuberculosis amongst hospital staff is added.

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ON ATYPICALITY AND THE DEPRESSIVE STATE.

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IT is perhaps not too fanciful an analogy to compare the expanse of psychiatric symptomatology to an expanse of sea scattered with a small and determinate number of islands.

These islands represent the typical cases of our psychiatric syndromes. To mention but a few: the anxiety hysteric with the bright smile and plethora of somatic dysfunction, the retarded melancholic, bearing all the guilt in the world on his shoulders, and the grimacing, hallucinated, well-established case of schizophrenia.

These cases are indeed the saving grace of the busy out-patient clinic, for dubiety is at a minimum, and the patient's physician can be advised in terms of a clear-cut diagnosis and almost certain prognosis.

Yet between these virtuous islands lie the channels of atypicality, replete with the whirls and eddies of uncertainty, carrying us first towards one island, and then sharply veering us towards another. It was perhaps inevitable that attempts should be made to group these islands. Mania and Melancholia in the unifying hands of Kraepelin readily became Manic-Depressive Psychosis. And indeed we must be grateful to him, although we may no longer *an seinem Feuer Süppchen kochen* for maintaining the concept of "disease entity" in an age which, under the stimulus of an adolescent Freudianism, might easily have become dominated by the doctrine of the *Einheitspsychose* to the detriment of our clinical and prognostic expediency.

Yet such groupings, almost as soon as formulated, split apart. For facts are formidable things, and symptoms are facts. A symptom is either present or absent, and although we may dispute its interpretation, its existence we may not dispute. Lewis (1), in his now almost classical paper on melancholia, did much to introduce us to a broader symptomatic conception of the depressive psychosis than was ever apparent within the rigidity of the Kraepelinian system.

Since 1934, when that paper was published, however, the advent of electrical shock therapy, although it has in no way altered the fundamentals of the situation, has given us the power of rapidly reversing the reaction, thus opening up a more extensive field of study. Indeed, the very availability and effectiveness of treatment have made many cases of mild depression seek earlier care, so that a shift in clinical emphasis has occurred away from the grosser types, which, in consequence, are becoming relatively less common. It is the purpose of this paper, therefore, to in some measure re-examine the

features of depression, and to relate them in particular to the problem of atypicality.

THE MATERIAL.

This study is based upon 130 consecutive cases admitted to Cheadle Royal, all individually investigated by the author. All were regarded as basically depressive, and the majority, spontaneously or under treatment, achieved complete and persistent remission of symptoms. Where this was not so is indicated in the text.

Sixteen, or 12.3 per cent. of this group were regarded as *atypical* within the terms of the following definition—"that although the psychosis was regarded as basically depressive, it showed sufficiently bizarre features, or such symptomatic loading with features of another reaction type, as to make it difficult to fit strictly within the bounds of the generally accepted criteria of the Depressive Reaction."

THE SIGNIFICANCE OF AGE AS A CRITERION OF TYPICALITY.

The problem of age in regard to the depressive psychosis centres principally around the question whether depressions occurring in later life show enough qualitative differences to justify their inclusion in a special category of involutional melancholia. No discussion of the validity of this contention is proposed in this paper, but it will be briefly touched upon in dealing with symptomatology. In order, however, that the qualitative differences and similarities between the depressions of earlier and later life may be more clearly seen, the entire series has been divided into two groups, on the basis of *age at first attack*. Those in whom the first attack occurred at the age of 45 or below have been arbitrarily designated *manic-depressive*, and those in which it occurred above the age of 45, *involutional*. The series broke, fortuitously, into two even groups of 65 cases each. The distribution of the atypical cases between the two groups is shown in Table I.

TABLE I.

	Manic-depressive.	Involutional.
Total cases in group	. 65	. 65
Atypical cases in group	. 15 (23%)	. 1 (1.5%)

THE SIGNIFICANCE OF HEREDITARY PREDISPOSITION AS A CRITERION OF TYPICALITY.

The significance of hereditary predisposition in mental disease is a difficult thing to assess with any degree of accuracy. There is probably no single factor in the patient's history which is more liable to distortion, either due to ignorance of the true facts, or their deliberate suppression. One gathers the impression (and it is only an impression) that the degree of eccentricity among the relatives of schizophrenics is higher than the incidence of positive mental disorder. This eccentricity in many cases seems almost to amount to an "abortive schizophrenia," and it is sometimes so definite that one has no

difficulty in deciding from which side of the family the illness is being transmitted. It is a factor, too, which because of its indefinite nature often escapes statistical evaluation.

The influence of heredity in the production of manic-depressive illness is, however, clearly established and recognized. It is particularly striking when one has access, for comparison, to the records of the present patient's relatives who have been in the same hospital anything up to fifty years previously.

Table II shows the distribution of mental disorder in the present series. Only positive factors appearing in the grandparents, parents, uncles, aunts and siblings were recorded, and only one factor was recorded in each case. When more than one factor was noted in the same history, a single factor was recorded in accordance with the priority indicated by the headings 1 to 8.

TABLE II.

	Typical (114).	Atypical (16).	Total (130).
1. Manic-depressive illness*	17	3	20
2. Suicide	5	1	6
3. Other psychoses :			
Nervous breakdown (un- specified) (5)			
In mental hospital (un- specified) (5)			
Psychosis, other than m a n i c-depressive (specified) (2)	12	..	12
4. Psycho-neurosis	2	..	2
5. Personality deviation (marked)	3	1	4
6. Alcoholism	1	..	1
7. Epilepsy	1	..	1
8. Mental deficiency	3	..	3
Total	44 (38.5%)	5 (31.25%)	49 (38%)
Psychosis only (1, 2 and 3)	34 (30%)	4 (25%)	38 (29%)

* *Manic-depressive illness* includes manic excitements, depressions of early life, involutional melancholia, and alternating states.

Kraepelin, quoted by Henderson and Gillespie (2), gives the hereditary predisposition in manic-depressive psychosis as between 60 and 80 per cent. This figure is presumably exclusive of involutional cases. Yet the overall average of the figures given in the above table would suggest a hereditary predisposition nearer to 30 to 40 per cent., that is to say about half that estimated by Kraepelin. Table III shows the distribution of hereditary pointers in the manic-depressive and involutional groups of the typical series (i.e. *excluding* the *atypical* cases), and even this only increases the disposition in the manic-depressive group to 44 per cent. (32 per cent. psychosis only).

TABLE III.

	Manic- depressive (50).	Involuntal (64).
1. Manic-depressive illness	4 .	13
2. Suicide	4 .	1
3. Other psychoses	8 .	4
4. Psycho-neurosis	2 .	..
5. Personality deviation	2 .	1
6. Alcoholism	.. .	1
7. Epilepsy	.. .	1
8. Mental deficiency	2 .	1
Total	22 (44%) .	22 (34%)
Psychosis only (1, 2 and 3)	16 (32%) .	18 (29%)

The difference between Kraepelin's figures and those given above is probably explicable on the basis of the divergent nature of the case-material. Taking the figures of naval cases given by Curran and Mallinson (3), admittedly covering the younger age-group, but in which approximately the same criteria of estimation were used, 29 cases out of 88 gave a positive family history, or approximately 33 per cent. Whilst no great degree of validity is claimed for the above figures, particularly as the number of cases in the atypical series is so far below that in the typical, yet they do suggest that the atypical group has a slightly lesser tendency to be hereditarily predisposed.

THE SIGNIFICANCE OF SYMPTOMATOLOGY AS A CRITERION OF TYPICALITY,

Table IV shows the general distribution of symptoms over the entire series.

The cases were principally classified according to their content. Obviously, no hard and fast division could be made, and mixed features occurred, but were less common than might at first sight have been expected. The allocation to a particular group of any one case depended upon an estimation of the symptomatology of the case taken as a whole, and on what features appeared to predominate. It is now proposed to examine some of those features in greater detail, first in respect of the 114 cases regarded as *Typical*, and then in respect of the 16 regarded as *Atypical*.

THE TYPICAL GROUP.

(a) *Depressive features*.—These were in the main examples or variations of the symptoms which have become recognized as peculiar to the depressive reaction. A sense of failure, ideas of regret over incidents in the past, direct expressions of unworthiness and self-depreciation or indirect expressions by exaggerating the goodness and admirable qualities of others. Expression of guilt for adolescent sexual activities such as masturbation or pre-marital or extra-marital intercourse, exposure to or acquisition of venereal disease, homosexual or other manifestations of abnormal sexual conduct. Concern

TABLE IV.

Content.	Typical (114).		Atypical (16).
	Manic-depressive (50).	Involutional (64).	
Predominantly	Depressive	36	51 6
	Somatic	8	12
	Phobic or obsessional	6	1
	Paranoid	..	 9
	Schizoid	..	 1
Anxiety*	43	64	 15
Emotional overplay†	17	23	 9
Retardation (marked objective)	15	7	
With anxiety	10	7	
With emotional overplay	3	..	
Pathological overactivity—			
Immediately prior to present depressive attack	5	2	
Recorded in the past	1	..	
Other symptoms—			
Hallucinations ; illusions	1	3	 4
Depersonalization ; derealization	2	7	 1
Perplexity ; confusion ; clouding	..	1	 6
Manneristic behaviour	..	..	 9

* Anxiety—simple anxiety symptoms, mild or severe agitation, panic, tension, apprehension, screaming fits.

† Emotional overplay—tears, spasmodic or persistent fits of weeping.

over past minor delinquencies was common, and often blame was accepted for topical events associated with the life of the patient, but entirely unconnected with any possible personal causation. Thus, one patient accepted blame for the illness of an old lady residing in her house who had had to be transferred to hospital. Indeed, the depressive mood may seem to encyst itself around any event, however remote, in the patient's life, or however topical. The environment, too—and this is a point often insufficiently emphasized—may be a source of distress and dissatisfaction. One patient objected to her cat looking at her, and turned her relatives' photographs back to front on the mantelpiece. A change of house often provides a source of querulous comparison of its evils compared with the virtues of the old. The reaction, on the other hand, may be virtually devoid of content. In one case in the series little or no content could be estimated because the mere approach of the physician produced a persistent flood of tears and a dramatic display of sobbing. In another case the whole psychosis centred round a set of ill-fitting dentures associated with a hysterical dysphagia and much emotional overplay.

Cases associated with much emotional overplay, particularly if they appear to arise out of an unsatisfactory life-situation and show apparent responsiveness to intercurrent stimuli, such as a physician's visit, are in danger

of being classified as "reactive," "neurotic," or in more contemporary terms, "topical," with a consequent playing down of their seriousness. No greater mistake could be made. The first patient quoted above before admission to hospital made several determined and almost successful attempts at suicide.

Several of the patients expressed the belief that they were influencing other patients. This rarely amounted to more than a vague feeling of adversely affecting them in some way, and in only three cases did it attain grandiose proportions. One patient stated he was doomed and a terrible scourge on the place, and expected to be thrown out. Another felt she was responsible for the nurses going sick, and stated that all the other patients had become worse since she was admitted. A third stated she had cancer and had infected all her friends, and was indeed responsible for all the cancer in the world.

Nihilistic delusions, especially of poverty, were perhaps the most characteristic feature of the involutional series, but again occurred in only a small proportion of that series (10 per cent.). The most characteristic feature of the younger group was the frequency with which they felt they were letting people down, husband, wife, family, or friends. One patient considered she was "deserting" her husband by coming into hospital for treatment, and two women with apparent sterility were mainly preoccupied by the way in which they were letting their husbands down by being unable to have children.

(b) *Somatic features*.—By far the commonest complaint consisted of pain or sensations referred to the head. This varied from frank headache, either frontal or occipital, to "disturbed feelings," buzzing sensations (not invariably associated with arteriosclerosis), pressure feelings on the skull, and a sensation of the head being enclosed in tight bands. Two patients referred to the sensation of numbness or "deadness" on the vertex. In only one case was it severe, and it was then associated with marked feelings of derealization and tended to be persistent.

Visual disturbances were common, but rarely amounted to more than a dimming or blurring of vision. Frank hysterical amblyopia was not noted in the series. One patient, however, complained of diplopia. This appeared a very unusual symptom not noted before or since. It was associated in this case with many other complaints and delusions of a somatic nature in a markedly hypochondriacal personality. It had appeared as a prominent symptom in each of the three major recorded depressive attacks which the patient had sustained over a period of 24 years.

Cardio-vascular symptoms consisted mainly of palpitation, sub-sternal pain and pseudo-anginal attacks, one patient complaining of his veins swelling as though they would burst.

Gastric symptoms were pain and peculiar sensations referred to the abdomen and stomach. Nausea was frequent, but in only one case was it associated with actual attacks of vomiting. Weakness and fatigue, sensations of vibration in the throat, loss of feeling in the arms, tingling sensations in the fingers, urinary dysfunction, cough and pain in the chest were all complained of. The more characteristic depressive beliefs of having acquired venereal disease or cancer and of undue preoccupation with the bowels were all in evidence. Gross hysterical features were noted in only 3 cases, all in the involutional

group: the case of hysterical dysphagia, already mentioned, one retarded melancholic who developed a hysterical monoplegia of the left arm, and one acutely agitated and confused patient with a hysterical paresis of both legs. These symptoms all cleared with the depression under treatment.

In the younger age-group one patient complained of being unable to breathe properly because she had become ultra-conscious of her breathing and required to "think out" each breath. This proved to be based on identification with her mother, who at that time was suffering from severe cardiac asthma, and whose illness was given as a principal reactive factor in the patient's history. This symptom, too, cleared satisfactorily with the depression under treatment.

(c) *Phobic and obsessional features*.—The association of compulsive features and depression is one of considerable interest, and has received some attention in the past. It is also generally recognized as being an association which is not uncommon, and for this reason, such cases as appeared in this series have been included in the typical rather than in the atypical group. The significance of the more purely phobic aspects, however, seems to have received little or no attention. Seven cases in this series (6 manic-depressive and 1 involutional) were regarded as predominantly phobic or obsessional in content. As these cases are of some interest, their principal features will now be briefly summarized.

CASE 1.—A recurrent retarded depressive state. The content of the patient's thought was entirely taken up with his preoccupation with several phobias the fear of heights, the wake of ships, and open razors. The wake of ships was associated with once seeing a man commit suicide by throwing himself overboard. The fear of razors was associated with once being shaved by a drunken barber. These fears were accompanied by brilliant visual images of almost hallucinatory intensity, and faded into the background with the depression under treatment.

CASE 2.—A meticulous, over-conscientious, neurotic personality, with a marked over-attachment to a tyrannical and psychopathic mother. She developed a retarded depression, in which the whole content centred around fears of what would happen to her parents if she died.

CASE 3.—Content of this case was almost entirely taken up with morbid thoughts associated with ideas of death, and she had vivid visual images of what she described as her own funeral.

CASE 4.—A notably depressive background was associated with a fear of pregnancy, coloured with obsessional doubts as to whether she was pregnant or not. The removal of the depressive element with treatment left the phobia of pregnancy relatively unaltered.

CASE 5.—A neurotic personality whose history revealed numerous phobias in childhood, of such things as moths and church. Over the last thirty years she had sustained several attacks of acute agitated depression with a predominantly phobic content, all apparently precipitated by some association with death. The death of a friend in the war, the unexpected death of a relative, seeing a man die suddenly in the street, and the death of a pet animal. During the attacks she became acutely afraid of going outside, going downstairs, and developed fears (not complaints) of bodily disease, for which she sought continual reassurance the effect of E.C.T. (and a more than average amount was given) was disappointing, for although it produced some improvement in the depressive element, the phobias tended to persist, and ultimately only became quiescent after the treatment had ceased for some time.

The last two cases are cases of depression associated with established obsessional neurosis.

CASE 6.—An excessively tidy woman addicted to washing rituals of moderate intensity, directed against faecal contamination. She visited a dying senile relative

and was shocked to see the bedclothes soiled with faeces. After the death of the relative, whose effects she had inherited, she became excessively worried about faecal contamination of this property and developed excessive rituals of washing, with a depressive state and some emotional overplay.

CASE 7.—A man married to a woman older than himself. His rituals and ruminations were associated with fire—cigarettes and matches—and he indulged in obsessional precautions about turning off the gas. After the death of his wife he went through a period of elation to an extent which caused comment by his friends, and in which the obsessional compulsions were less insistent. This was followed by an attack of depression in which the obsessive features altered. Some turned into phobias projected into the past of more obviously depressive emphasis (e.g. he began to wonder if he had harmed some of his childhood friends), associated with more typically depressive ideas such as wondering whether his brain was diseased.

In only one other case in the series were obsessional features prominent. This patient was obsessively preoccupied with words and their derivation. These words would come into his head and he would link them with obscene associations, then being afflicted with a compulsion to say the words aloud. In this case also there was misinterpretation of a paranoid illusionary variety in that he heard the wireless accusing him of a number of misdeeds such as sexual perversion, violence and murder. The depressive element in this case, however, appeared dominant, and the pre-psychotic personality, although meticulous and obsessional in type, showed no actual symptoms of a florid obsessional neurosis. Treatment removed the depression and other symptoms.

This patient would correspond to the type mentioned by Stengel (4), in his recent observations on the relations between depression and obsessive-compulsive symptoms, where patients with marked obsessional personality features, but not actually suffering from an obsessional neurosis, develop severe obsessional features in the course of their depressions only—a type which, he points out, is often diagnosed as a recurrent or cyclical obsessional neurosis. One would merely point out in passing the significance of this observation in connection with states referred to as “recurrent paranoia.”

In attributing to depression an unmasking and aggravating effect on latent obsessional symptoms, one could carry this viewpoint to its logical conclusion by ascribing to depression an exaggerating effect on all the attitudes and attributes of the personality, so that the appearance of hypochondriacal, paranoid, phobic, obsessional and hysterical symptoms may be expected during the course of a depression in the appropriate personality.

This would present us with a so-called “dynamic” relationship of relative simplicity. Yet it is hardly possible to extract the depressive element from the totality of the psychic situation unless one is willing to give it an independence, perhaps even a physiological independence, outwith that situation. To do so would be to strike at the very roots of psychic causality, upon which any system of psycho-dynamics must inevitably be based. If the concepts of psycho-dynamics are to remain as useful in the future as they have been in the past, their mechanisms must be regarded as interdependent in a logical and not merely incidental way. This, of course, does not make it impossible to accept the view of a physiological concomitant of the depressive state, of which view the rational psychiatrist in this modern age must, Janus-faced, be ever aware.

It means simply that one must regard the psyche as a more or less fluid equilibrium, reacting to a total situation in which the depression, if it appears, is given purpose and meaning. Thus, Stengel notes that there are obsessional neurotics who are subject to recurrent depressions, but rejects the explanation that these depressions are the natural reaction to an exacerbation of the obsessional illness. Yet cases can be cited in which the presence of strong external factors may succeed in upsetting the delicate dynamic equilibrium of the obsessional system with the logical appearance of depression.

Two cases (not included in the series, as they were seen elsewhere) may be quoted in this respect: A young married woman of markedly obsessional personality, excessively house-proud, within a few weeks of having her first baby developed a depression with much weeping and emotional overplay. The baby formed a disruptive element in the obsessional system, making the obsessional rituals less easy to carry out. She was much preoccupied with cleaning rituals and avoidance of faecal contamination, and admitted that from the first she found handling the baby's excreta distasteful to her, in spite of her attempt to overcome it. The second case was of a nurse who, before her marriage, was associated with infant welfare work. In this case the patient had twins. Of a markedly obsessional personality, she accepted the rituals of infant welfare work with the rigid conscientiousness which would be expected of such a personality, until she had to put them into practice in the case of her twins. The impossibility of carrying out this task to her satisfaction led to a depression of the same type with much emotional overplay. Indeed, one can hardly think of a more closed or vicious circle than is illustrated by these two cases.

Imagine for a moment an experimental situation in which, as part of that situation, an obsessional neurotic is forcibly prevented from carrying out customary rituals. Surely this would lead to intensely aggressive behaviour directed towards the frustrating object? In the cases quoted above the frustrating object is at one and the same time the loved object, and hatred directed against the loved object is the very essence of obsessional ambivalence. The unconscious hatred directed against the child would lead to a reinforcement of the defensive rituals which are *ab initio* the very protection against such hatred. The frustrating effect of the child, however, remains, and although in actuality perhaps no greater in degree, would have the effect of an intensified challenge to the intensified defensive rituals. This in turn would lead to an increase in the unconscious hatred directed against the child, with the development first of an anxiety situation. Thus a position would soon be reached in which the intensification of the defensive rituals might no longer be able to keep at bay the unconscious hatred against the child, which would come dangerously near to full conscious expression. As conscious hatred against the loved object is in this case intolerable, the depressive position soon intervenes in which it finds conscious expression against the patient herself, in an overwhelming sense of guilt, and in which the obsessional mechanisms, as they are now no longer necessary, fade into the background.

It is significant that in both cases the depression was possessed of the same quality, a weepy state with much emotional overplay and practically devoid

of content—a condition suggestive of Stengel's "masochistic orgy," but probably as near to a "pure" depression as it is possible to go.

Thus, between the purely obsessional position and the purely depressive, a series of stages may intervene. There may be a stage of partial reinforcement. This would explain the appearance of more formal obsessional symptoms in the obsessional personality with depression; and the intensification of obsessional rituals in the frankly obsessional, associated with an element of depression which often does not appear to predominate (Case 6). From a stage of partial reinforcement a more completely depressive position may be reached in which the obsessional content becomes more obviously replaced by a depressive content (Case 7). The final stage would be that of descent to a "pure" depression virtually devoid of content (i.e. devoid of rationalizations and elaborations). These conclusions must be regarded as largely tentative, and they cannot be elaborated further at this stage, although it is hoped to do so in a future communication. In the five obsessional states quoted in this section a clear-cut external situation was present in them all, and all it is desired to emphasize at this point is that factors in the external situation should not be entirely ignored in presenting a truly dynamic view of the relationship between obsession and depression.

(d) *Paranoid features*.—As Lewis (1) has pointed out, paranoid beliefs are not uncommon as part of a depressive illness. They vary from simple referential delusions obviously based upon guilt feelings, to more marked delusions of a persecutory nature in which the accompanying attitude is less one of resignation as one of hostility and resentment. The list given below shows the gradation in type of the paranoid beliefs throughout the typical series. Most of the beliefs were of the simple referential type, as cases which showed prominent paranoid beliefs had by definition fallen within the atypical group.

1. "People were looking at her strangely, talking about her, and criticizing her."
2. "Her appearance had deteriorated and people were laughing at it and talking about it." (This patient was markedly narcissistic.)
3. "She was being shunned by everyone because it was known that she had been her fiancé's mistress."
4. "People were talking about his strained relationship with his wife, and discussing his homosexual tendencies."
5. "His friends were talking about him."
6. "People were making a fool of him."
7. "She was going to be done away with."
8. "A mockery was being made of him, and he was being represented on the screen."
9. "He was to be prosecuted because his accounts were wrong."
10. "The police were going to take him to prison because he struck his sister."
11. "He was being watched by the pension people." (Believed he had accepted a pension under false pretences.)
12. "People were laughing at her and spying on her."

13. "People thought he was a spy and police agent."
14. "His removal to hospital had been organized by the state police."
15. "People were following him, and he was to be taken away and tortured. He was under arrest and in prison."
16. "His foreman was against him."
17. "Her family were against her."
18. "The window cleaner had stolen a wheel-barrow, and the people next-door were guilty of wrong-doing." (Associated with marked agitation.)
19. "A doctor (who had taken off a sample of blood) had injected poison into his system. As the doctor had been a Jew, he was now a Jew-hater. There was an organized conspiracy to remove him to hospital." (Agitation.)
20. "The Nazis were after him." (Agitation.)
21. "His guts were being strangled in the night; he was dead and was going to be taken away by embalmers. The embalmers were persecuting him." (Agitation.)

The problem of practical importance is to decide how much significance should be placed on the appearance of paranoid beliefs in the course of an apparently depressive illness. Obviously if too great a relevance is placed on the superficial symptomatology of a psychosis, without reference to the underlying affective state, whether the symptomatology be obsessional, phobic, paranoid, or schizoid, then the way is open to prognostic uncertainties of no small magnitude.

This is a point which cannot be too strongly emphasized, because it is felt that routine diagnosis is still too often a matter of being impressed by what is obvious in the content without its being related to the underlying emotional state. Thus bizarrerie is "schizophrenic" whether, indeed, schizophrenia is present or not.

Yet it is not always easy to nullify the paranoid element. A patient who appeared to be suffering from a typical "melancholic" depression was heard to remark that "she was illegitimate and had been brought to hospital in the Royal Car, and the King had been talking to her." This statement seemed to bear a grandiose quality verging on the paraphrenic. It was only some days later, when she was heard asking whether she was fit to be a patient in this "Royal hospital," that it was realized that her previous statement had been one of extreme humility, and the "Royal" car was the hospital car and the "King" the Medical Superintendent. In the second case the patient felt that people were looking at him, and his friends shunning him because of an alteration in his facial appearance which made him ugly and ape-like. Yet in this case there was undoubted depression, showing a characteristic diurnal variation in intensity, with a pyknic build and an active energetic pre-psychotic, personality. The "paranoid" feature here was regarded as largely self-depreciative and in harmony with the emotional state.

A depressive reaction with a paranoid content does not appear to be a precursor of a true paranoid state, certainly not a common one. Paranoid states often have an associated depressive element. Yet the distinction is almost always clear-cut, and there is usually no difficulty in deciding when the paranoid element is dominant.

(e) *Miscellaneous symptoms*.—Apart from the illusions and visual images in connection with the phobic and obsessional features, only two examples of actual hallucinations were found in the typical series, both in the involuntional group. One patient heard voices which he attributed to the departed spirits of his ancestors telling him to pull himself together morally—a clearly self-accusatory phenomenon. While in another case, a voice repeating over and over again, “What shall we do? What shall we do?” was an obvious expression of the patient’s agitation and distress. Feelings of depersonalization and derealization, although not restricted to the involuntional series, were most commonly associated with it. Feelings of depersonalization were of two types. Expressions of having changed in some way, of feeling different, of complete loss of feeling, or inability to feel, of being a different person, were common. The more bizarre and less usual type was difficult to dissociate from what were virtually gross somatic delusions, e.g. :

“His heart had burst open and the blood was rushing to his head and giving him pain.”

“His stomach was an empty cask, devoid of feeling.”

“He was half in and half out of the ward, and the food he was eating was passing through all the other patients first.”

“His body had ceased to function below the neck.”

Feelings of derealization were, on the whole, very much less prominent, but when they did occur, had a quite characteristic quality.

“Everything was dull and bleak, and the world had lost its colour.”

“The world was in four sections in contradistinction to each other.”

“The beauty had fallen away from the world like petals from a flower.”

(f) *Anxiety*.—In discussing anxiety in relation to the depressive state it is not proposed to revive the acrimonious arguments of “psychosis” *versus* “psycho-neurosis” which flourished in the nineteen-thirties. Such distinctions have frankly lost significance under the modern therapeutic urge, which is less concerned with allocating to the case a rigid diagnostic label than in estimating the total reaction, in an endeavour to assess which form of treatment is likely to be most beneficial, whether it be psycho-therapeutic or physical. To revert to the analogy of the introduction, it is not that the “islands” have become less important, but that they have become land-marks as well as landing-stages.

Anxiety in one form or another, either objective or subjective, is almost universally associated with depression, as can be clearly seen from Table IV. It is for this reason that the tendency to sub-classify depressions on the basis of anxiety is to be deprecated. Lewis (5), in a more recent account of depression, regards it as being of two types, melancholia and agitated depression, each type having a minor form, the minor form of melancholia being simple or neurasthenic depression, and that of agitated depression being anxiety state. Munro (6) would retain the older categories of manic depressive depression and involuntional melancholia, while adding a further group of anxiety depressions.

Such classifications may be a matter of clinical convenience, but as it is obvious that any classification is bound to be unsatisfactory, it would seem

better to speak simply of the depressive state or depressive reaction, while using such generally accepted terms as "agitated depression," "retarded depression," etc., in particular cases as implying shorthand descriptions rather than specific sub-types.

Of the 7 cases in the typical series in which anxiety was not recorded, 5 were associated with marked retardation almost amounting to stupor. In the other 2 the depression was associated with a marked degree of apathy, and both showed little effective or sustained response to treatment. They appeared to be acquiring all the characteristics of chronicity.

(g) *Retardation*.—Retardation was only recorded in this series if it was marked and objective. As seen from Table IV, it was more often than not associated with definite anxiety and even with emotional overplay in the form of tears or fits of weeping. The "characteristic" and often perpetuated picture of the severely retarded melancholic as dry-eyed and without objective anxiety clearly does not fit in with these facts. Further, 7 cases occurring after the age of 45 showed definite retardation. No history of a previous attack of depression could be obtained in any of them. This illustrates the difficulty of assigning special characteristics to depressions occurring at the involutional period of life—at least sufficiently standardized to enable them to be regarded as separate entities.

Retardation appears not only to imply a depth of reaction, but a particular quality of reaction apparently closely allied to endogenicity. This is indicated by Table V.

TABLE V.—*Relation of Hereditary Pointers to Retardation.*
Typical Series—114 Cases.

	No.	Positive family history.	
		Psychosis only.	Total.
Retarded . . .	22	8 (36%)	10 (45.5%)
Unretarded . . .	92	26 (28%)	34 (37%)

THE ATYPICAL GROUP.

(a) *Paranoid features*.—In this group they assumed a more persecutory character, often associated with definite ideas of influence. Heightened suspicion and perplexity went hand in hand with an alteration in external reality, in which undue significance was given to events and objects in the patient's surroundings. The different quality of the features can be seen by comparing the list given below with that given under paranoid features in the typical series. The paranoid features, too, in this group, appeared to occupy a considerable portion of the total content of the reaction rather than being merely incidental.

1. His work-fellows were trying to gas him, and since he had come into hospital gas was being pumped into his bed. The workmen had stabbed him in the back with a syringe, causing spots and pain.

2. He was being accused of having venereal disease, and if he went to the

pictures he found this fact being related on the screen. He also found references to it in the newspapers. Society was against him, and people were accusing him of wrong-doing.

3. The Boys' Brigade were being paraded outside the window to spy on her. The nurses and doctors were trying to poison her, and figures of men were being kept in the ward to frighten the patients.

4. She was being hypnotized through cigarettes, and the objects in her room were being altered in a peculiar way. Her clothing was being destroyed, and an attempt was being made forcibly to separate her from her husband.

5. People were acting towards her in a strange way, and names and signs on the road had been altered.

6. He was being influenced by electricity.

7. "They" were laughing at her.

(b) *Schizoid features*.—True schizophrenic behaviour or thought was only prominent in two cases, and in only one did it reach such proportions as to make the diagnosis of a depressive state in doubt. This patient was of pyknic build, had a positive history of manic-depressive disorder in one parent, and was normally (if one may say so) a somnambulist. He passed through a period of acute depression with clear-cut ideas of guilt and suicidal tendencies, to arrive at a detached and mildly disordered state (he tied padlocks and keys to his shoes), in which Divine commands came into his head instructing him to go on journeys. The whole condition cleared with complete insight under electroplexy. In the second case the patient expressed the belief that her thoughts were coming from the wireless.

(c) *Manneristic behaviour*.—The patients in this group showed every form of disordered behaviour, restlessness, grimacing, talkativeness, repetition of stereotyped or obscene phrases, gesticulation in a dramatic and theatrical manner, adoption of peculiar and grotesque postures, speaking in an affected, childish or pedantic voice, rearranging objects and clothing, mutism, resistiveness, negativism, and aggressive behaviour, contradicting forcibly statements made to them (often apologized for afterwards, when well), laughing and weeping in turns, singing, whistling and over-breathing. All associated with a marked depressive element in which tears, regret and a hopeless outlook could readily be detected.

(d) *Depersonalization and derealization*.—This was only prominent in one case, and attained considerable proportions, the patient believing she was an abnormal person, a monster created by God, and indestructible, so that she would never die, but was, in addition, full of disease for which there was no cure. The hospital was cut off from the outside world and the people in it were not able to leave, and if they did so, they only left in their minds, their bodies remaining behind.

(e) *Hallucinations and illusions*.—Two patients had hallucinations of smell for odours coming from their own bodies. One stated he was giving out an odour obnoxious to his friends, and another complained of the smell of blood on her hands. Two of the patients were in a restless state, and afflicted with extensive visual and auditory hallucinations. One heard a voice repeating the same phrases over and over again, and saw faces with no body attached. This

patient also had visual images of some intensity associated with her thoughts! thus, if she thought of a telephone a persistent image of one would appear.

The second patient heard people crying for help, and heard his wife's voice coming from odd corners of the room. He also saw people staring at him through the window, and believed he could read people's thoughts and summon spirits.

It may therefore be seen that the criteria on which the atypicality of this group was mainly judged consisted of markedly paranoid features with a persecutory quality, heightened suspicion, perplexity and ideas of influence, grotesque and manneristic behaviour, and a marked hallucinatory activity. Truly schizophrenic features, such as basic thought disorder, were practically non-existent. It is important that this should be recognized, however, as these cases might have been classified as "schizophrenic" or "paranoid," on the basis of the bizarre quality of the ideas of depersonalization and derealization, the erratic behaviour, the hallucinations and paranoid features, the depressive element being readily obscured by the prominence of the superficial symptomatology. The apparent similarity between these states and such delineated series as the "Schizophreniform" of Langfeldt (7) and "Schizo-affective" of Kasanin (8) is too obvious to require elaboration. These states also showed marked episodicity with complete remission of symptoms between attacks, and no apparent tendency to dementia. Some were seen after having sustained repeated attacks over a period of as long as twenty years. Nine members of the group had had attacks prior to the one studied, and of these one had 1, four 2, two 5, and two 6 previous attacks.

THE SIGNIFICANCE OF PERSONALITY AS A CRITERION OF TYPICALITY.

The problem of personality is by far the most difficult factor to analyse in relation to mental disorder. No mere listing of traits would provide an adequate study, for the personality, whatever its constituents may be, is essentially the integrated psyche in action. It is only desired, therefore, to draw attention to some general features which appeared to arise from the study of the cases in this series.

There appeared little justification for the view noted, particularly among analytical writers (9), that there is a unitary "depressive personality." The personalities in this series, once detached from the complicating features of the depression, showed considerable variability so that no possibility of success could be claimed for any attempt to force them all into the same mould. It is true, however, that if one is prepared to ignore the more individual features of the personality pattern, and concentrate only on what might be termed the "field of action" of the personality, certain striking features emerge. These are detailed in Table VI.

The restricted personality was the commonest manifestation, and was more in evidence in the involutional than in the manic-depressive series. It was characterized by much conscientiousness, a reserved ultra-sensitive disposition, the whole expressing itself within a narrow field of interest. This type of personality has been regarded as "inhibited," but this is scarcely an adequate

TABLE VI.

Personality type.	Manic-depressive (50).	Involucional (64).	Atypical (16).
Restricted . . .	23 (46%) .	53 (83%) .	7 (44%)
Active . . .	8 (16%) .	4 (6%) .	2 (12%)
Inactive . . .	2 (4%) .	3 (5%) .	..
Neurotic . . .	17 (34%) .	4 (6%) .	7 (44%)

description. Within the narrow field the activity may be extensive, but directed towards a few over-valued ends and ideals, or to the maintenance of certain exaggerated standards. It is the failure to attain such ideals, often beyond their inherent capacity, or their unadaptability to the fluctuating demands of external reality, that lead, in these individuals, to a breakdown with depression. Naturally the contrast between what it has been desired to achieve, and what has actually been achieved, make the involucional period of life a particularly vulnerable one for such personalities. But as what has actually been achieved is often of an above-average standard, these individuals appear to be, and indeed are, social assets. There is, therefore, some justification for the aphorism that depression is an illness of "valuable people." The personality is rigid, however, and devoid of much of the resilience necessary to meet the everyday ebb and flow of life. In some respects it might be regarded as "obsessional," but to term it so is probably carrying it a stage too far.

The instinctual energy has become diverted into the narrow channels of certain personal ideals, and in so far as their attainment is socially useful, and in that they show little evidence of reaction-formations of a truly obsessional type, it is probably wiser to refer to the personality as simple restricted.

The active group consisted of bright go-ahead energetic individuals in whom mood swings were not much in evidence, and whose life seemed to consist of a mild hypomanic attack punctuated by episodes of usually severe, but often infrequent, depression.

The inactive group was made up of a melancholy, brooding, self-pitying, lugubrious personality type, relatively infrequently encountered over the entire series. These two latter groups were obviously the most closely related of all to the manic-depressive constitutional tendency.

The neurotic group was entirely heterogeneous, consisting of neurotic, obsessional, psychopathic, inadequate, and poorly integrated personalities. As might be expected, they made up a high proportion of the personalities in the atypical series, and as such personalities under stress are more liable to breakdown earlier in life, they also formed a not inconsiderable fraction of the manic-depressive group.

It is fully recognized that the analysis of the personality given above has many imperfections, but it is only intended to convey a general and not intimate, or even particularly accurate, picture. In assessing the personality for allocation to a particular group, however, it was decided to ignore what Fox (10) has termed the "thymopathic factor" (manic-depressive constitutional tendency). From a study of this series it seemed to possess a somewhat elusive quality, it being more often possible to say when it was present than when it was not. It seemed to run through certain of the cases like a thin red line, and because

of its dramatic qualities, especially in alternating states, it tended to obscure the basic features of the individual personalities which, when dissociated from it, and from the complicating features of the depression or excitement, showed considerable variability.

THE CLINICAL AND ETIOLOGICAL SIGNIFICANCE OF DEPRESSION AND ITS RELATION TO ATYPICALITY.

The problem which this paper has been mainly designed to present is to what extent it is justifiable to introduce the concept of atypicality into a consideration of the depressive state. Melancholia is a field in which many claims have been staked in the past, claims built mainly upon half-truths. the relationship between excitement and depression involved in the concept of manic-depressive psychosis, for example. Fox found only 21 per cent. of his 400 cases had had an excitement, or history of excitement, and the figure in the present series would be much less. The relationship of body physique to depression is also true, but only up to a point, and the manic-depressive constitutional tendency is certainly a factor, but little more.

It would seem, therefore, that we have turned full circle from the classical concept of melancholia, through that of manic-depressive psychosis, to that of the depressive state, with the concept broadening from the symptomatic point of view. Thus in the typical series we have not only to account for depressive and somatic features, anxiety, retardation, personality and reality disturbance, but also for illusions, hallucinations, hysterical, paranoid, obsessional and phobic symptoms. Further, if the atypical series are regarded as valid, manneristic and grotesque behaviour, vivid hallucinatory states, marked persecutory and even schizoid features, have to be added.

Such bizarre reactions were included in the category of depressive states on the following grounds :

1. The prevailing affect was persistent and essentially "depressive," or, if it could not be so clearly defined, at least, "unpleasant."
2. The states were self-limiting, or responded to electroplexy, with complete remission of symptoms, and absence of residual dementia.

It can be seen, therefore, that we have gone little beyond the concept of the depressive state formulated by Lewis (1), except perhaps to include some rather more atypical cases than were given in his series. The cynical may feel that we have gone little beyond the prognostic-diagnostic criteria of Kraepelin, "If it gets better it is depression; if it doesn't, it is schizophrenia, paranoia, or what you will." Yet, regardless of its superficial symptomatology, there is something fundamental about the depressive state, just as there is something fundamental about true process symptoms in schizophrenia. We know now that, although a depressive reaction is liable to occur in a particular type of personality, it is not the prerogative of that type, so we need not be surprised if the superficial symptomatology of the reaction varies towards the limits of the atypical members in this series.

Is it necessary to emphasize that the depressive state, or depressive reaction, implies more than depression? That it implies persistence and self-limitation,

for example. It would appear to be necessary to do so. Good (11) would have us believe that there are two types of depression, melancholic and schizophrenic. Depression appearing in diverse clinical states, such as G.P.I. or schizophrenia, cannot be regarded as unusual if one regards depression as a normal psychological phenomenon. But can there be any logical basis for the view that depression differs in quality, when it appears in different pathological states, or indeed differs in any other way than in extensity or intensity, or both?

Its extensity or intensity being dependent upon the circumstances under which it is arising and on the nature of the pathological processes at work. Good would see these processes as stages in a basic insanity, an *Einheitspsychose*, leading to a state of complete ego disintegration.

Yet as equally convincing an argument could be produced for a basic organic pathology if one took only cognizance of the relatively limited number of changes that are possible in tissue cells. Surely, however, the patterns are important? They not only show the quality inherent in the basic material, but provide the key to the nature of the causal factors.

Jefferson (12), in his recent Lister Oration, stated that he suspected that discussion of mind-brain relations would always be premature. One suspects the same may be true of the *Einheitspsychose*.

SUMMARY.

1. The clinical features of depression have been re-examined in the light of 130 cases.
2. It is suggested that the broader symptomatic view, propounded by Lewis requires emphasis and extension.
3. It is further suggested that the more atypical features arise mainly in poorly integrated or eccentric personalities who break down early in life and tend to be slightly less hereditarily predisposed.
4. A critique of depression as a "symptom" and as a "reaction" is given.

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THE CONCENTRATION OF ADENOSINETRIPHOSPHATE (ATP) CITRATE AND CALCIUM IN BLOOD DURING INSULIN SHOCK THERAPY

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CONCENTRATION changes of blood constituents other than glucose occurring during hypoglycaemia, and particularly during insulin shock therapy, have been studied by several authors (e.g., Harris, Blalock and Horwitz, 1938; Katzenelbogen et al., 1939) though not always with concordant results. One of the most constant features of insulin hypoglycaemia is a decrease in the level of inorganic phosphate during the phase of blood-sugar fall and a gradual return to normal after the blood-sugar curve has reached its lowest value. This fact which was described soon after the discovery of insulin (see Cori (1931) for a review of the older literature) is generally attributed to the increased phosphate esterification consequent upon the enhancement of glucose utilisation and is in harmony with the current concept that the function of insulin is primarily that of a promotor of glucose phosphorylation.

It seemed of interest to study the level of adenosine triphosphate (ATP) in blood during insulin-shock therapy in view of its intimate connection with glucose phosphorylation. The maintenance of an adequate rate of glucose phosphorylation and that of an adequate level of ATP are mutually interdependent processes, at least in isolated enzyme systems, and a fall of either one or the other might initiate a dangerous vicious circle. Since Olsen and Klein (1947) reported a fall in the concentration of ATP in the brain of hypoglycaemic cats it is important to know how general this phenomenon is. The ATP of blood which is entirely intracellular (Kerr and Daoud, 1935) is metabolically very active with a turn-over rate as high as the ATP of liver (Hevesy, 1947); it may therefore be expected to reflect to some extent the ATP-metabolism of the majority of tissues.

The citric acid content of serum was studied because citric acid may be involved in the hypoglycaemic syndrome for two reasons: as a member of the tricarboxylic acid cycle it is linked to glucose metabolism and it is also intimately connected with calcium metabolism and through it may be influenced by the concentration of inorganic phosphate.

Finally, serum calcium levels were investigated in a small number of cases because of the connections with phosphate and citrate metabolism. Serum calcium levels have previously been studied, but with conflicting results: whereas Accornero and Bini (1937) reported a decrease in hypoglycaemia, Georgi (1936) found increases and several other authors (Beiglböck and Dussik,

1937 ; Harris et al., 1938 ; Katzenelbogen et al., 1939 ; Delay et al., 1945) came to the conclusion that there was no significant change.

METHODS.

The subjects were chosen at random from the patients undergoing insulin shock therapy at this hospital. They received an individually adjusted dose of insulin designed to produce hypoglycaemic coma 3-4 hours after intramuscular injection ; it varied from about 40 units to about 250 units. Four venous blood samples were collected from each subject : (1) before insulin injection ; (2) two hours after injection ; (3) during coma, and (4) one hour after termination of coma. In the series of calcium determinations a fifth sample was collected one hour after insulin injection.

Serum was used for the analysis of citric acid and calcium. For the estimation of ATP 5 ml. blood were drawn up into a syringe and immediately delivered into a graduated, glass stoppered cylinder containing 20 ml. ice cold trichloroacetic acid (20 per cent.). This procedure minimises the enzymatic breakdown of ATP after the withdrawal of blood.

Estimation of ATP.—ATP was determined in the trichloroacetic acid filtrate by the increase of inorganic P produced by purified myosin which specifically converts ATP into adenosine diphosphate (ADP) and inorganic phosphate. Phosphate liberated by myosin will be called the "myosin-P" fraction. In addition the fraction hydrolysable by *N* HCl in 10 minutes at 100° C. (the "10'-P" fraction) was determined.

Phosphate estimations were usually done by the method of Berenblum and Chain (1938). Sometimes the less laborious, but less accurate method of Fiske and Subbarow (1925) was used.

A detailed description of the analytical procedure follows. The trichloroacetic acid filtrate was measured and 1 ml. *N* HCl was added. The acid solution was extracted four times with 10 ml. portions of peroxide-free, redistilled ether to remove excess trichloroacetic acid. The volume of the extracted solution was again read and, after neutralisation, ether was removed by evacuation and gentle warming in a water bath. After the volume had been made up to 20 ml. or else noted down, inorganic and 10'-P fractions were determined in suitable aliquots (1 ml. for inorganic P and 0.5 ml. for 10'-P fraction, when the Berenblum and Chain method was used ; with the Fiske and Subbarow method fourfold quantities are required).

Myosin was prepared from rat muscle essentially according to Bailey (1942) with some modifications. The skinned and eviscerated carcass of a rat was packed in cracked ice for 15 minutes. Sufficient muscle was excised and passed through a cooled Latapie mincer to collect 10 g. of ground tissue. This was immediately suspended in 50 ml. of cold solution of 0.5 *M* KCl + 0.03 *N* NaHCO₃ and gently stirred for one hour at 0°. The pH was maintained at 7.0-7.5 by adding a pinch of solid NaHCO₃ once or twice during the first 10 minutes. The centrifuged extract was clarified by filtration through a layer of paper pulp, diluted with 200 ml. of ice-cold glass-distilled water and brought to pH 6.8 by the addition of *N*/10 HCl. The precipitated myosin was immedi-

ately centrifuged and redissolved in 30 ml. of the $\text{KCl}-\text{NaHCO}_3$ solution. Precipitation by dilution with 200 ml. water and solution in 30 ml. $\text{KCl}-\text{NaHCO}_3$ was repeated until the protein had been three times reprecipitated. No acidification is necessary after the second and third dilution. The final precipitate was stirred up in 15 ml. $\text{KCl}-\text{NaHCO}_3$ solution and the total volume measured. Solid KCl was then added to bring the concentration up to 0.5 M whereupon the remaining precipitate was easily dissolved. It is important for the preparation of active extracts to keep the temperature as low as possible, to use glass-distilled water throughout and to avoid delay during the process of reprecipitation. The preparation remained sufficiently active for at least a week when kept at 0° . For use it was diluted with an equal volume of 0.2 M glycine- NaCl buffer of pH 9.1.

The estimation of "myosin-P" was carried out in two test tubes each containing a 6 ml. aliquot of the ether-extracted neutral filtrate and in addition 0.2 ml. of 0.1 M CaCl_2 ; 1.8 ml. 40% trichloroacetic acid was added to one of the tubes, followed by the addition of 2 ml. myosin in glycine buffer to both. After 30 minutes incubation at 37° the same amount of trichloroacetic acid was added to the second tube. The "myosin-P" fraction is given by the difference of the P-values.

Estimation of citric acid.—Three ml. serum were added slowly to a mixture of 20 ml. water, 3 ml. 10 per cent. sodium tungstate and 3 ml. 0.67 N H_2SO_4 . A 20 ml. aliquot of the filtrate was concentrated on a hot-plate to a volume of 2-3 ml. and analysed by the method of Weil-Malherbe and Bone (1949). The petroleum ether extract was shaken with 1 ml. Na_2S solution in a centrifuge tube and, after short centrifugation, an aliquot of the aqueous layer was transferred to the micro cell of the Spekker absorptiometer with the aid of a fine-tipped teat pipette.

Estimation of calcium.—The method of Wang (1935) was used.

Blood sugar was estimated by the method of Nelson (1944).

Tests of statistical significance.—In each group the analytical results represent four or five series of values of which one value in each series is contributed by the same individual. If the means of two series were compared on the basis of the variance of the two series, the values would be treated as random samples and no account would be taken of the pairing of values. The tests of significance were therefore based on the variance of the differences of two paired values x_1 and x_2 and t was calculated by the following formula:—

$$t_{(n-1)} = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\frac{\sum(x_1 - x_2)^2 - (\sum x_1 - \sum x_2)^2}{n(n-1)}}}$$

where $\bar{x}_1$ and $\bar{x}_2$ are the means of the two series of values x_1 and x_2 and n the number of differences.

RESULTS.

Blood-sugar values were determined in a large number of cases in this and other series of investigations. The lowest level of blood sugar, varying from

practically 0 to about 20 mg per cent., is usually reached two hours after the injection of insulin. The onset of coma takes place 1-2 hours later when the blood sugar has either remained unchanged or has shown a slight rise. One hour after the termination of coma the blood sugar has reached a more or less normal level again. The detailed communication of these figures has been omitted in view of the wealth of similar data in the literature.

The analyses of inorganic P, myosin-P and 10'-P, contained in Table I, show that there is a marked fall of the inorganic phosphate level two hours after insulin injection reaching an average of about 70 per cent. of the pre-injection value. During coma, i.e. 3-4 hours after the injection, the level has risen again to about 82 per cent. and in the fourth series it has practically returned to normal. The differences between the means of these series are all significant.

The level of ATP, as measured by the myosin-P fraction, remains practically constant two hours after insulin injection. In the two following series the ATP concentration increases to 110 and 116 per cent. above the initial level. Both increases are significant (comparison was made between series 2-3 and 2-4).

This increase is not shown, however, by the figures of the 10'-P fraction; on the contrary, there is a significant decrease in the second series. Later, a return to the pre-injection level is observed.

The last four columns of Table I show the percentage of 10'-P accounted for by ATP, as determined by the myosin method. It is obvious that the mean figures are all significantly below 100 and that ATP does therefore not, as is often assumed, account for the entire 10'-P fraction. In the pre-injection sample ATP accounts on the average for only about 80 per cent. of the total 10'-P fraction, but under the influence of insulin the percentage increases and reaches a value of 90 in the last sample. This increase, too, is significant. The other component or components of the 10'-P fraction have not been identified, but since the ATP fraction increases at the expense of the unknown residual fraction (the total 10'-P fraction remaining constant) it presumably consists largely of ADP.

Table II contains the results of citric acid analyses carried out on 22 cases. In some of these the blood for citric acid analysis was drawn at the same time as the sample for the estimation of ATP. These cases bear the same serial number in Tables I and II. In spite of greater individual variation the differences of the mean values of the four samples are small. Yet there is a significant decrease from the first to the second sample, followed by a significant increase from the second to the fourth sample. It may be concluded that there is a slight fall of the citric acid level during the first phase of hypoglycaemia, amounting to 15 per cent. on the average, and a return to a near-normal level after termination of the coma. In some cases (No. 1, 14 and 20) a further sharp drop occurred in the fourth series.

The serum calcium was investigated in only eight cases (Table III). The fall of the calcium level during hypoglycaemia, though quantitatively small, is highly significant statistically. There was considerable variation of the time at which the lowest calcium value was observed. Sometimes the minimum was reached as early as one hour after insulin injection, in other cases only

during coma. For the evaluation of the significance of the change occurring during the whole period of hypoglycaemia the lowest of the three values obtained in series 2, 3 and 4 was selected and compared with the initial and final value.

DISCUSSION.

Of the concentration changes described the fall of inorganic phosphate is quantitatively the greatest. It is also that which is probably most directly connected with insulin action since an increased rate of phosphorylation is a necessary preliminary to an increased rate of glucose utilisation. It is in agreement with this interpretation that the level of inorganic phosphate tends to rise again as soon as the phase of rapid glucose utilisation is ended and the blood-sugar level has dropped to a stable value. The blood-ATP remains

TABLE I.—*The Concentration of Phosphate Fractions in the Blood of Patients in insulin shock treatment.*

Sample 1.—Withdrawn before insulin injection.

Sample 2.—Withdrawn two hours after insulin injection.

Sample 3.—Withdrawn during coma.

Sample 4.—Withdrawn one hour after termination of coma.

Case No.		Inorganic P (mg./100 ml. blood).				Myosin-P(mg./100 ml. blood).					
		Sample				Sample					
		1	2	3	4		1	2	3	4	
I	..	..	3.19	1.90	2.75	3.80	..	2.69	2.59	3.07	3.21
2	..	..	4.50	3.14	4.21	4.38	..	2.15	2.20	2.34	1.97
3	..	..	4.26	3.28	3.47	4.08	..	3.01	2.70	2.76	3.20
4	..	..	4.72	2.93	3.44	4.86	..	3.42	2.66	2.99	2.83
5	..	..	4.78	3.10	3.80	5.17	..	2.05	2.57	2.61	2.49
6	..	..	3.92	3.27	3.28	4.03	..	2.13	2.08	2.15	2.24
7	..	..	3.65	1.75	2.22	3.47	..	2.24	2.25	2.71	3.40
8	..	..	2.62	1.53	2.32	3.52	..	2.10	2.68	2.61	2.35
9	..	..	4.81	3.71	4.35	5.45	..	2.25	2.46	2.51	2.75
10	..	..	3.73	2.41	3.54	4.44	..	2.32	2.21	2.68	2.91
11	..	..	3.79	3.46	3.52	4.07	..	2.96	2.34	2.79	3.33
12	..	..	4.92	3.20	3.74	3.90	..	1.97	2.13	2.04	2.30
13	..	..	5.11	3.27	3.09	3.82	..	2.57	2.27	2.74	2.86
14	..	..	3.52	2.64	2.64	3.05	..	2.14	2.30	2.44	3.10
15	..	..	5.36	4.34	4.18	4.75	..	2.53	3.08	3.35	3.61
16	..	..	5.80	3.82	4.50	4.08	..	3.07	3.15	3.65	3.83
17	..	..	3.59	2.94	3.39	3.90	..	3.40	3.03	3.34	2.88
Mean	..	..	4.25	2.98	3.44	4.16	..	2.53	2.52	2.76	2.90
Standard error	..	..	0.205	0.181	0.099	0.151	..	0.116	0.080	0.103	0.125
t*	..	..	10.62	4.64	6.07	..	..	4.73	3.62	..	..
p	..	..	< 0.01	< 0.01	< 0.01	..	..	< 0.01	< 0.01	..	..

* Calculated from the differences of paired values, see "Methods."

TABLE I—*continued*.

10'-P(mg/100 ml blood)						$\frac{2(\text{Myosin-P}) \times 100}{10' \cdot \text{P}}$				
Sample						Sample				
	I	2	3	4		I	2	3	4	
I	..	5.40	4.96	6.03	7.01	..	99.9	104.5	101.6	91.5
2	..	5.64	5.41	5.01	4.92	..	76	81.3	93.7	80.2
3	..	8.34	6.62	6.43	6.90	..	72.3	81.6	86	94.5
4	..	7.28	6.37	6.34	6.60	..	94	83.5	94.5	86
5	..	7.60	6.60	7.05	7.16	..	54	78	74	69.5
6	..	4.58	5.19	5.56	4.61	..	93.2	80.3	77.3	97.3
7	..	4.94	4.96	5.46	5.98	..	91	90.6	99	113
8	..	6.51	5.37	7.96	4.78	..	64.5	100	65.6	98.5
9	..	5.57	5.89	6.25	6.33	..	80.7	83.5	80.4	87
10	..	6.21	5.58	6.56	6.84	..	74.5	79.3	81.6	85.2
11	..	5.59	5.17	5.74	6.75	..	106	90.5	97.5	99
12	..	4.03	4.30	4.06	4.52	..	98	97	101	102
13	..	7.08	7.01	6.70	8.05	..	72.5	64.8	81.8	71.1
14	..	7.96	5.90	8.84	7.11	..	53.8	78	55	87
15	..	7.09	7.18	7.80	7.75	..	71.4	87	86	93
16	..	9.0	7.88	8.95	8.74	..	68.2	80.0	81.5	87.7
17	..	7.77	8.10	6.61	6.61	..	87.5	75	101	87
Mean	..	6.50	6.03	6.56	6.50	..	79.8	84.5	85.8	90.0
Standard error	..	0.342	0.261	0.313	0.295	..	3.80	2.37	3.21	2.61

		←————→		←————→		←————→		←————→	
t*	..	2.55	2.06	2.163	..	3.086			
p	..	0.025	0.06	0.05	..	< 0.01			

* Calculated from the differences of paired values, see "Methods."

constant during this phase indicating a balance between the rates of phosphate transfer and rephosphorylation. The subsequent rise of ATP concentration seems to be at the expense of the ADP-fraction. It indicates a preponderance of the synthetic reaction and may be attributed to the accumulation of organic phosphate esters.

Studies with P_{32} have demonstrated that insulin increases the rate of ATP turnover in muscle (Sacks, 1945; Goranson et al., 1948). In liver, insulin raises also the concentration of ATP (Kaplan and Greenberg, 1944). On the other hand, there is a decrease of ATP and an increase of ADP in the brain of hypoglycaemic cats (Olsen and Klein, 1947), which presumably results from the exhaustion of carbohydrate fuel and the consequent depression of metabolism in this tissue. The high level of ATP stores in liver, blood and other tissues may contribute to the rekindling of brain metabolism during recovery from hypoglycaemic coma.

The slight fall of serum calcium may also be connected with the lowering of the inorganic phosphate level and may be an expression of the tendency to keep the Ca : P ratio constant.

TABLE II.—*Concentration of Citric Acid in Serum of Patients during Insulin Shock Treatment.*

Sample 1.—Withdrawn before insulin injection.

Sample 2.—Withdrawn two hours after insulin injection.

Sample 3.—Withdrawn during coma.

Sample 4.—Withdrawn one hour after termination of coma.

Case No.	Citric Acid (mg/100 ml serum).			
	Sample			
	1	2	3	4
1	2.81	2.25	2.75	2.07
2	1.18	2.14	2.05	2.37
5	1.85	1.51	1.31	1.31
6	2.30	1.84	1.98	2.03
7	1.91	1.41	1.63	1.83
8	1.01	0.71	0.91	1.13
9	1.74	1.39	2.00	1.63
10	2.03	1.93	1.84	1.69
11	1.11	1.09	1.31	1.35
12	2.69	2.17	2.17	2.24
13	1.86	1.45	1.40	1.47
14	1.93	1.65	2.07	1.21
15	1.21	1.45	1.19	1.59
16	1.88	1.45	1.80	2.08
17	2.22	2.41	1.98	2.67
18	2.52	1.79	2.31	2.33
19	1.92	1.49	1.01	1.92
20	2.51	1.91	1.81	1.26
21	2.99	2.46	2.22	3.02
22	1.24	0.72	1.02	1.21
23	2.00	1.48	1.91	2.25
24	2.15	1.99	1.72	2.25
Mean	1.962	1.668	1.745	1.860
Standard error	0.119	0.102	0.101	0.111

t*		3.704	1.123	2.52
p		< 0.01	0.30	0.02

* Calculated from the differences of paired values, see "Methods."

The fall of serum citrate may be considered in relation to the virtual disappearance of blood sugar. It may be argued that the failure of glucose supply will eventually lead to a lowering of the level of the metabolic stream fed by it which will affect all derivatives. However, the disappearance of circulating glucose is in the first place due to an opening of the sluice gates and the filling of the stream to capacity. Thus, one would expect an increase rather than a decrease in the level of oxidative metabolites, at least in the first phase of hypoglycaemia while glucose is still being absorbed by the tissues.

TABLE III.—*Concentration of Calcium in Serum of Patients during Insulin Shock Treatment.*

Sample 1.—Withdrawn before insulin injection.

Sample 2.—Withdrawn one hour after insulin injection.

Sample 3.—Withdrawn two hours after insulin injection.

Sample 4.—Withdrawn during coma.

Sample 5.—Withdrawn one hour after termination of coma.

Case No.	Calcium (mg./100 ml. serum), Sample				
	1	2	3	4	5
25	9.8	9.9	9.6	9.9	10.3
26	11.9	11.1	11.1	10.3	12.4
27	11.6	10.3	10.4	10.4	10.8
28	9.4	9.2	8.9	9.0	9.8
29	10.2	9.7	9.7	9.4	10.2
30	10.6	9.8	10.0	10.2	11.0
31	10.0	9.6	9.4	10.2	11.0
32	11.2	10.3	9.4	10.0	11.3
Mean	10.59	9.99	9.81	9.92	10.85
Standard error	0.317	0.204	0.242	0.172	0.282
$\longleftrightarrow$ $t^* \dots \dots \dots 4.79$ $P \dots \dots \dots < 0.01$ $\longleftrightarrow$ 5.78 < 0.01					

* Calculated from the differences of paired values, see "Methods."

The fact that the fall of citrate occurs early in hypoglycaemia suggests that the explanation must be sought elsewhere. It is possible, e.g., that this change is linked with the changes of calcium and phosphate concentration. The connections of citric acid and calcium metabolism have long been recognised and Alwall (1945) has shown that the concentrations of both substances in serum often move in the same direction.

Natelson et al. (1948), in experiments which came to the writer's notice after the present work had been completed, found a decrease of serum citric-acid levels after glucose intake and also, in a series of six cases, after insulin injection. In both cases the drop amounted to about 30 per cent. Although this effect is larger than that observed in the writer's cases the results are in general agreement.

SUMMARY.

The blood content of adenosine triphosphate (ATP) and the serum content of citrate and calcium has been studied at various stages before, during and after hypoglycaemic coma and the following observations are recorded:—

(1) In accordance with previous investigators it is found that the curve of inorganic phosphate has fallen by about 30 per cent. two hours after the injection of insulin, but then again moves upwards and has reached normal levels one hour after the termination of coma.

(2) The level of ATP is unchanged two hours after insulin injection, but shows a slight increase later.

(3) ATP accounts for 80-90 per cent. of the "acid-labile" phosphate fraction. As the concentration of ATP increases, that of the unknown residual component decreases. It is suggested that the residue unaccounted for by ATP may consist partly or wholly of adenosine diphosphate.

(4) There is a slight fall of serum citrate during the first phase of hypoglycaemia amounting to about 15 per cent. on the average and a return to normal after termination of coma.

(5) There is a fall of serum calcium during hypoglycaemia which is quantitatively small, but statistically significant.

(6) The changes are discussed and it is suggested that the drop in citrate concentration may be connected with the changes in phosphate and calcium metabolism rather than with changing levels of other glucose metabolites.

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RECENT DEVELOPMENTS IN INDUSTRIAL SELECTION TECHNIQUES.*

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INTRODUCTION.

THIS paper is chiefly concerned with the recent developments in industrial selection techniques at these works. However, below its chocolate covering, I hope you will find that its centre, although still recognisably confectionery, contains ingredients, varied in origin and possible other use, possessing, if properly masticated and adequately digested, fundamental values not specific to chocolate.

INFLUENCES SHAPING THE PROCEDURES.

Before going on to describe to you the current practices of the Selection and Training Department in this organization, I should like to indicate very briefly what has mainly influenced us in shaping these procedures. To the established personnel policy of this company as outlined by Seebohm Rowntree in *The Human Factor in Industry*, the psychologists in the Personnel Division owe their existence of course. This foresight I wish only to acknowledge before describing the forces that have chiefly influenced us in the last three years. These are the psychological research in the field of mental measurement, the personnel selection procedures of the Army and the Navy from 1942, recent studies in industrial mental health and, lastly, the present-day labour supply in this area.

Psychological research in the field of mental measurement has not been confined to test construction and test experimentation. Much work has been done on studies of the reliability and validity of these instruments of mental measurement so that there is available for the practising industrial psychologist very many well tried statistical devices with which to examine his procedures. The examination of testing programmes with such statistical procedures as the calculation of correlation coefficients—particularly in examining reliability and validity of the testing procedures—and analyses of variance and covariance (with particular reference to the grouping of data) has resulted in the rejection to the rubbish heap of a fair collection of imposing psycho-physical apparatus and shattered many dearly held beliefs of the significance for prediction purposes of many aspects of human behaviour.(1) So-called tests of aiming, steadiness, finger reaction and endurance, on electrical-contact apparatus and dynamometers have not survived an examination of the relationship between

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test and re-test scores. Furthermore, factor analysis methods of studying the inter-correlation of test results and job performance have provided a means of indicating on the one hand the extent to which performances on apparently dissimilar tests are expressions of one ability, and on the other hand, the pattern of human abilities involved in doing satisfactorily a particular industrial task.

The net practical results of our own application of the research worker's statistical methods are (1) we have very much reduced the number of psychophysical tests used in our selection procedures; (2) we know a group of our tests can be combined to give a measure of a practical ability somehow related to efficiency in the workrooms, and (3) a short test of verbal intelligence is a useful component in a selection battery used in this organization.

Statistical mathematics are a fascination in themselves and some notion of them is essential to the establishment of technically sound procedures. From the application of selection techniques in practice, however, much is to be learned in terms of administrative convenience and practical feasibility. In this direction the psychologists at the Cocoa Works, as elsewhere, owe a great deal to the widespread use of psychological techniques of selection in the Armed Forces during the war.

From the industrial psychologist's point of view the greatest effect of the services' procedure has been the publicity accorded psychological selection methods. I am not referring to the correspondence columns in *The Times* and *Telegraph*, but to the spread of knowledge of selection tests among those who took them. In our daily contact with present and future employees we meet few men who have not already had personal experience of the kind of procedure we have adopted. This in the great majority of cases is a great help. Furthermore, the services showed that within agreeably acceptable limits it was possible to apply sound selection procedures to large numbers in a short time. This has naturally brought the industrial psychologist to pay attention to considerations of administrative convenience in his design of procedure. Those techniques of academic psychology that make great demands on the time of subject and examiner are not appropriate in employee-employer situations. Somehow or other the psychologist must fit his procedure into the existing administrative machinery of engagement procedure. Two further influences of service experience are related to details of practice. The first of these is the use of standard biographical questionnaires suitably designed to contain information supplied by the candidates, interviewer's notes and data for record and research purposes. The second is the importance placed on the interview—not only as a means of eliciting information about the candidate, but as a final opportunity to ensure that the candidate is fully informed on every aspect of the many possibilities of the selection proceedings—to this is closely associated the importance to good selection of obtaining the candidate's co-operation in choice of job where a choice is available. A last lesson from services selection procedure relates to the evidence provided by certain Naval investigations(2) in which it was demonstrated that psychiatric screening within an acceptable range of errors either way could be carried out by lay assistants given appropriate training in "spotting."

The possibility of this screening is important in view of the recent findings of that important contribution to industrial mental health—Russell Fraser's report on incidence of neurosis among factory workers. This report undoubtedly implies a need for careful personal interviewing of applicants for work and for careful examination of jobs for the demands they make on workers not only in terms of physique, intelligence and aptitude, but also in terms of social interaction with which an inability to cope constitutes, in greater or less degree, what has commonly become known as instability. The service investigations and the Russell Fraser report have together contributed to the shaping of that part of our present procedure concerned with questions of personal stability in a factory environment.

Overriding all other influences in the development of our procedure is that of the demands made on our services. Naturally we are attempting to provide the service called for. It might appear at the present time in York (and, indeed, in very many other parts of the country) that as long as there are fewer candidates than there are jobs there is no need for specialist services in the field of selection. But in my view psychological methods are being used at their best in just such a situation—in which the problem shifts from "which few of these many shall I have" to "what is the best possible way of matching these few to the jobs available."

THE PROCEDURES DESCRIBED.

Having made that brief introductory acknowledgment of some of the influences that have shaped it, I should like now to go on and describe our selection procedure in detail.

Procedures have been evolved to meet the following requirements:

Selection and placement of beginners in the factory (girls, boys, women); the assessment of beginners in the offices (girls, boys, women and men); the selection of apprentices (building and engineering trades only); assessment of applicants for promotion in the factory; assessment of applicants for staff appointments (promotion candidates, depot managers, technicians, salesmen, etc.).

In all cases three distinct tools are employed: First, a biographical questionnaire completed by the candidate; secondly, an individual interview; and thirdly, appropriate standardised psychological tests. The use of these together constitutes a fairly recent development in selection techniques in a private firm, although the National Institute of Industrial Psychology has been making use of the combination in its vocational guidance work for a very long time and is at present doing much to spread its use throughout industry.

The biographical questionnaire we use is a single sheet, foolscap size, with a 2-inch blank margin down the right-hand side and a 3-inch section at the bottom marked "Do not write here." This section contains a row of 12 mystic letters. Beside each of the first seven of these the interviewer enters a query (?) if during the interview there has come to light anything unusual with reference to work record, attitude to health generally, eating and sleeping in particular, powers of endurance, feelings of sensitiveness, relations with the

police. The last five refer to height, weight, vision, colour vision and handedness. Below these hieroglyphics is a table for the entry of test results.

The rest of the form has, in addition to a section at the top asking for name, address, age, date of birth, married or single, four sections. These relate to the occupation, education, recreation and social contact activities of the candidate (i.e. membership of youth organizations and clubs and experience of controlling other people).

In Section 1—occupation—the form covers candidate's present job, how long at it, job wanted here, relatives and friends here, time in Services and rank held; there then follows a blank section in which the interviewer traces the candidate's work history from age on leaving school—given in the next section—to present age, recording time spent on each job and the reason for leaving.

In Section 2—education—the questions relate to name of last school, age on leaving school, class, certificates won, training since leaving school.

In Section 3—recreation—the instructions are: "Underline any of the following things you do or have done in your spare time, add any other hobbies you may have." Then follow three columns of items and a column of blank lines. In the first column are mainly activities of a practical nature (mechanical repairs, woodwork, painting, etc.), the second mainly aesthetic and intellectual (music, reading, discussion), and the third mainly physically active (games, swimming, etc.). The blank lines are for the addition of interests not quoted.

Section 4 is concerned with the social contacts of the candidate, asking him if he was a member of clubs or youth organizations, if ever in charge of someone, if he has ever taught anyone anything.

This form is completed by the candidate with the aid of one of the department's technical assistants. It is important that this assistance is at hand at this time.

The candidate then does whatever tests are appropriate. Before discussing these in detail I should like to go to the next step in the procedure—the psychologist's interview, as this is closely tied up with the form's design.

This interview does not follow a particular sequence, but the ground covered is well defined. This has already been indicated by the biographical questionnaire on which the interview is based. It is the interviewer's aim to supplement the contents of the form, noting special points in the blank margin and conclusions in the blank space at the bottom. It is usual to get the candidate to give a brief *résumé* of his school, work and service career, to expand on the interest items underlined, to describe his family background and his general health over the last five or six years. The contribution of the interview to the selection procedure is two-fold. First, it provides additional information in the way of personal explanation on the actual attainments and experience of the candidate. Secondly, it provides the evidence upon which some picture of the candidate's disposition can be formed. It is on the interview entirely that we depend for clues of an instability likely to limit a candidate's industrial usefulness. Instability may be inferred from either verifiable facts about the candidate or, less tangibly, the attitude adopted in relation to certain topics. The facts we have found bearing useful clues to instability are those relating

to job record (many jobs with poor reasons for leaving), reduced social contacts (no clubs, no friends, or close associates), few interests (no games, hobbies, pets, etc.), no roots (no regular home contact or family associates), and, in contrast, overwhelming domestic responsibility. The subjects to which too emotional an attitude is a danger signal are ill-health, sleeping and eating, and lack of physical endurance.

I do not want to emphasize this particular aspect of our selection procedure, but it is of interest that we find about a third of our women candidates need special consideration for placement and follow-up on these grounds—this figure is similar to the proportion of women in industry reported by Russell Fraser as having suffered from neuroses.

The final step in the interview is to try as far as possible to come to some agreement with the candidate on the kind of job for which he or she is best suited.

That, with minor adjustments to suit the case, is a brief indication of the part played by the interview in each of the selection procedures I have mentioned. Whatever the job, it is desirable to have a well designed biographical questionnaire on which all data on a candidate can be assembled, which can be used in the competitive situation as the basis for candidate comparison, and later, in all cases, as the instrument for records and research.

SELECTION PROCEDURES AT DIFFERENT LEVELS.

Whatever the job, it is sound personnel practice to know all there is to know of the employee's occupations, education, recreation and social contacts. Consequently our programme of biographical questionnaire and individual interview by a psychologist is the same for all jobs—beginners in the factory, beginners in the offices, apprentices in the engineering and building departments, promotion candidates in the factory and applicants for staff appointments. The testing practices, however, vary considerably. I should now like to describe the tests we use at these different levels.

The Selection and Placement of Beginners in the Factory.

This is the area of our activities in which most research has been done on testing procedures. Girls and women, before engagement, take a battery of psychological tests which cover (1) intelligence, (2) practical ability for factory purposes, (3) strength of grip, and (4) specific aptitude for certain types of factory jobs.

The use of tests for the selection of factory operatives is not a recent development in industry, but their systematic use for all entrants, including those for non-competitive vacancies, is unusual in this country. The actual battery used here is unique, containing components devised and standardized at these works.

The intelligence test has been introduced to give a rough assessment of intelligence—we are interested in knowing whether an applicant is in the top 5 per cent. or bottom 5 per cent. of the factory population—for both of which sections we think rather special placing and training is required. This, we

believe, a short ten-minute intelligence test might tell us accurately enough. It is, however, very difficult to construct a reliable short test. The one we have produced contains 17 items of the completion type :

Hot, cold; up, down; in . . .

11, 9, 7, 5, . . .

It has a high reliability within itself and a very high correlation with one of our longer intelligence tests. Its shortness gives it a great deal of value in terms of administrative convenience.

The so-called practical ability test is the combined scores of two card-sorting tests, the Seguin Form board and a specially designed form board. The test scores are totalled because analysis has shown that the four tests measure much the same qualities, though in varying amounts. The name given to the summed score—practical ability—seems a reasonable description from the performance nature of the component subtests and from the fact that there is a significant positive correlation between the battery's total score and the efficiency of workers assessed in terms of quarterly outputs.

To measure strength of grip we use the dynamometer—taking a measure of the strength of grip of the dominant hand. There is an area of work in the factory for which a weak grip renders the operative unsuitable. The test/re-test reliability of this instrument is not as high as would be desirable.

Now for three new tests which have recently been designed for the specific purposes of assisting us in the placing of candidates in one of three broad groups of factory jobs. It is possible to go over all the jobs in a factory and classify them in a variety of ways—physical requirements, mental requirements and so on. It is also possible to classify them according to differences in the conative elements of the working situation—that is, differences in the striving aspect of the situation. In this respect a large proportion of our factory jobs can be classified accordingly as the operative is :

(a) Being fed by a machine.

(b) Feeding a machine.

(c) Assembling by hand individual units to form larger units.

(In the first, things are coming at you and you are striving to do something about it; in the second, you are striving to push things into the ever-opening jaws of an insatiable monster, and lastly, you are sitting by yourself striving to keep at it, putting little things together into bundles.)

So we have devised three analogous test situations.

(1) The candidate stands at a conveyor belt arrangement and turns the knobs of passing units.

(2) The candidate feeds with her hands wooden plates to a semi-automatic machine that she operates with her foot, so that a plunger may be directed through the holes in the plates.

(3) The candidate is given sets of imitation chocolates and cartons and asked to pack the chocolates into the cartons.

Now these three tests make, we believe, a sensible finish to the selection procedure. Their relevance to jobs in our factory is obvious. Although the tests can be scored and although they have been proved reliable and shown to be in some measure valid for selection purposes they have an additional value

as media through which the candidate can express a personal preference for kind of factory work. Whether preference for a test is a reliable guide to suitability for an analogous job is a subject we are now investigating.

That is the group of tests we use for factory entrants—women and girls. For boys and youths the three analogous tests are replaced by a standardized arithmetic test, since arithmetical attainment to a certain level is the *sine qua non* of success of a whole group of jobs filled by boys and youths—packing and stores, stores control, sampling, etc.

Office Entrants.

The tests used for office entrants are exclusively paper and pencil tests of intelligence, arithmetic attainment, English attainment and a so-called clerical aptitude—this last consists of exercises in coding, sorting and checking a whole mass of clerical detail. The intelligence test in this group is the standard test used for all promotion selection procedures and staff appointments. It is a verbal test of 38 items and has a time limit of 20 minutes. It has been standardized on a factory population of over 1,000. Its validity in this organization is shown in the differences of distribution of scores in different working groups—significant differences existing among factory men, apprentices, chargehands, office entrants and staff applicants.

Apprentices.

Vacancies for apprentices are offered from time to time in open competition. The screening is done by the paper and pencil tests of intelligence, arithmetic and English, used for office entrants. For each vacancy three candidates are entered on a short list. The boys chosen for this then go through a series of interviews by the employment manager, education officer and foreman of the appropriate department, and each candidate does a series of practical tests with these gentlemen looking on. This, I may say, is done informally—about four or five boys working at the same time in the room and the observers just wandering around. The tests are:

(1) A set of assembly problems from putting together six simple interlocking links of a chain to the assembly of a valve that has 11 separate parts.

(2) Manual dexterity test that consists of screwing and unscrewing a set of nuts and bolts.

(3) A peg board test that consists of fixing a number of small pegs in a wooden board.

The final selection of apprentices is made by a committee of the observers—foreman, education officer, employment manager, psychologist—after consideration of *all* the data collected. The results of these tests are only part of the evidence.

Promotion and Staff Vacancies.

For promotion candidates in the factory and applicants for staff appointments the only tests used have been our standard intelligence test and some kind of group situation tests.

Although the details of the latter varies slightly with the vacancy under consideration we have over the last two years evolved a pattern of procedure that appears to be giving satisfaction to candidates and managers alike. A group of six candidates are invited by letter to take part in a group selection test on a given date, being invited to York the evening before to meet two of the company's officials socially in the "local," where they are introduced to each other and have a meal together. In the morning at the works the programme consists of series of discussions among the candidates with the interested parties sitting in the background.

The first is a leaderless discussion in which a general problem involving the handling of a mass of material—packets of goods, loose goods, correspondence files, detailed analysis of some commercial situation and so on. The candidates are given some specific problem relating to these and asked to work out a solution. They are allowed to go on at this for about half an hour. It is not, however, expected that they should have reached a solution in that time. Each candidate then in turn takes the chair of a committee composed of the other candidates and in his own words sets the committee on to discuss a topic provided. In each case there is some specific instruction to the committee—e.g. "A youth Centre is to be set up in an industrial area. You, as representative citizens are asked to say how such a centre should be planned and what it should provide." "Many boys aged 17-18 have applied for deferment of, or exemption from, military service. Your committee is asked to devise a set of rules for the guidance of tribunals dealing with such applications."

At the end of the morning exercises the candidates go to lunch with members of the staff of the department in which the vacancy exists, who are about the level at which the successful candidate will be entering. The afternoon is spent in a series of individual interviews and the writing of reports by each candidate of the meeting he conducted in the morning.

The development in selection technique represented by this group procedure is not without its dangers. Certainly the procedure breaks down the nervousness and cautious reserve of most candidates and induces the observer to match one candidate against another, time after time, for an appreciable period till preference crystallizes, but it is, I think, a matter of some concern that the dynamic group discussion part of the programme makes so much stronger an appeal to the layman than more objective selection methods. The collection of factual evidence by interview and other means, such as by psychological testing and the analysis of the requirements of the job, are more laborious tasks than forming a preference for one of an observed group, and are, therefore, in danger of being neglected or relegated to an insignificant place in the total selection procedure.

If this new technique in social behaviour study led in selection work to an ignoring of the factual evidence of a candidate's ability from other sources and the omitting of an analysis of the job itself with a view to finding the best possible match of candidate to job, then it would not, in my view, be a progressive development.

REPORTING THE CONCLUSIONS.

I have described to you three tools of modern industrial selection and illustrated the use of psychological tests at a number of different industrial levels. You will appreciate that the provision of efficient tools is not enough ; a practical plan of action must also be devised, to ensure their use. As far as the factory is concerned the Selection and Training Department, which uses the techniques I have been describing is informed from day to day of the current factory vacancies and endeavours to match the current supply of candidates to these vacancies—as it is responsible for the training of these beginners in their factory jobs this matching is done with all the care possible. In the competitive situation where there is a number of candidates for one post, the department's practice is to endeavour to encourage the manager concerned to make the selection himself on the basis of all the evidence that can be amassed—the data from the psychologist on each candidate being presented in a brief non-technical report. This deals with the candidate's personal appearance, with notes on physical attributes ; a brief history of his achievements in school, leisure and work, and in the Services with a comment on whether this is above or below the average of candidates for the post under consideration ; an assessment of his intelligence and an opinion on the quality of his ideas, his powers of expression ; a note on any special aptitude (mechanical, mathematical, musical, etc.) ; a description of his chief interests with an indication of any emphasis—practical, physically active, intellectual, aesthetic or social. This is followed by an attempt to describe the general disposition of the candidate in terms that are relevant to most industrial situations—from what has been gleaned from the candidates in interview, tests, group discussion—how may he be rated for (a) dependability (does he complete things, has he achieved much starting from little, can he be relied upon ?) ; (b) acceptability (does his school, work and Service career and sparetime activities indicate that he is the kind of man other people have accepted readily ?) ; (c) dominance (does his past history show any evidence of a bias in favour of taking a leading part or a submissive role in the groups to which he has belonged ?).

The report concludes with a description of the candidate's background, upbringing and his present domestic situation. A note of general comment is added tying the whole thing together and drawing out contrasting and complementary features of the report to illustrate suitability for the vacant post.

With such reports on each candidate the manager is then in a position to match candidate with candidate and even to arrange them in an order of preference. It is important for the sake of the successful candidate's future career that he should be firmly established in the manager's opinion as the best available candidate for the job and not be a nominee of some external authority.

CONCLUSION.

These, then, are some of the recent developments in industrial selection procedures with which we are acquainted in Rowntrees.

You will appreciate that all I have said about selection techniques in industry must be considered against the background of some industrial organization. Selection procedures lie within a company's personnel policy. Only in so far as that policy is a sound one in every respect, and is conscientiously put into effect throughout the organisation will success attend the application of selection procedures of the kind I have described.

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CONSTITUTIONAL FACTORS IN INSTITUTION CHILDREN.*

By FRANK BODMAN, M.D., D.P.M.,
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I AM deeply conscious of the honour you have done me in asking me to serve as your Chairman for the coming year. I feel this promotion is somewhat premature and that there are others better qualified for this responsible task. But I bow to your wishes and will do my best to serve you.

I feel rather ambivalent about the tradition which rules that there is no discussion of the Chairman's address, as I would prefer to stimulate a debate, and I have chosen for my subject this evening a field of study where there is plenty of room for argument. I hope therefore that even if you cannot voice your disagreements with me now, on some other occasion we may be able to resume the debate.

Having completed early this year an investigation which has occupied most of my spare time for some three or four years, I have had a few months to reflect on the results, and am venturing to put before you the results of my meditations. You may possibly dismiss them as a "blinding glimpse of the obvious," but they are based on this survey, which has substituted a scientific method for an intuitional one.

Briefly, the object of this investigation was to ascertain the kind of social adaptation made by children brought up in institutions, when they left school and the institution, and began to earn their living.

At the time of the promotion of the investigation in the spring of 1943, the war had emphasised the necessity for making provision in this country and in Europe for homeless, abandoned and unwanted children. Because of the size of the problem it was believed that many of these children would have to be placed in institutions, and it seemed of the utmost importance to ascertain whether the institution child suffers from disadvantages in his development as a person, in comparison with the child brought up in a normal home. It was a general impression among those who have to deal with children that the child brought up in an institution compares unfavourably with the child who has had the benefit of normal home surroundings, but in this country, this was an impression only, and not based on scientific enquiry. It is true that about this date Dr. Edelston had published in America his studies on the effects of hospitalisation in children (a survey which he had begun in 1938). But hospitalisation, while it involves the factor of separation from the parents, is not the same situation as institutionalisation.

In America, as early as 1940, the concept of the "institution child" as a clinical type had been developed and elaborated. Lowrey, while working as a psychiatric consultant to an orphanage, was impressed by the compara-

* Chairman's Address, Child Psychiatry Section of the R.M.P.A., read 19th July, 1949.

tively uniform pattern of socially disturbing behaviour, in a series of children referred for advice from the orphanage; he attributed this maladjustment to a common factor—that of being reared for approximately three years in a home for infants. This prompted a study of all cases referred from infants' homes for two years, and a series of 28 children were accordingly investigated. Lowrey claimed that only those children admitted before the age of two developed the syndrome of personality distortion, characterised by unsocial behaviour, hostile aggression, inability to give or receive affection, inability to understand or accept limitations, and marked insecurity in adapting to environmental changes.

This pioneer investigation of Lowrey's was followed up in America by a series of more detailed investigations by Goldfarb. This worker made a comparison between children who had spent the first two or three years of their lives in institutions, and then had been boarded out, and compared them with a control group whose total experience had been in foster homes. In this first study 40 institution children, average age six years plus, were compared with 40 foster home children of the same age.

It was clearly demonstrated that the institution children showed greater frequency of problem behaviour, more expression of anxiety—restlessness, hyperactivity, inability to concentrate—more open expression of aggressiveness, such as temper tantrums, impatience, obstructiveness, cruelty without cause, disregard of other people's rights. It was inferred that the institution children were less secure, more isolated from other people, and less capable of entering into meaningful human relationships.

In another study, it was shown that institution children were more predisposed to poor adjustment in a foster home, and to transfers to further foster homes because of unusual behaviour. The problems that made replacing necessary were aggressive, hyperactive behaviour, bizarre, unreflective actions, and emotional unresponsiveness.

Goldfarb considered these investigations left him with the definite inference that the emotionally deprived infancy of the institution child resulted in a dramatic arrest in all aspects of his (personality) development, and in the formation of a characteristically typical personality.

Was this childhood pattern permanent? Goldfarb (1943) then investigated 15 children (average age 12 plus) who had entered institutions in very early infancy and remained there three years before transfer to foster homes, and compared them with a control group of the same age who had always been fostered out.

His findings were that "the institution child continues to be different from a group of family children, even as late as adolescence, and even after a long period of foster-family and community contact. The institution child has a personality which has not expanded to the same degree. In the realm of the intellect, his behaviour is more aimless, thoughtless, unplanned, wasteful. In the realm of feeling his responses are poor and meagre. His range of language is narrower, his pronunciation imperfect."

"The absence of human ties, particularly the absence of relationship with protecting, loving adults, leads to personal insecurity. The institution group

is consequently characterised by the need for attention and affection. Yet the never sated craving for affection is accompanied by the inability to set up a mature give-and-take relationship.

"The fact that the personality-distortions caused by deprivation are not overcome by later family and community experience must be stressed," he writes, "if anything, there is a growing inaccessibility to change."

After further controlled studies of institution children at three years and eight years, Goldfarb (1945) undertook intensive investigations of the life histories of 15 institution adolescents—a longitudinal section after his series of cross-sections.

In his view these studies confirmed the inferior intellectual performance of the institution child. In his view they cannot grasp ideas about space and time, and so disregard temporal and spatial limitations. "They don't keep on the pavement, wander on the way home from school, don't come in at bedtime. They cannot recall the past clearly or anticipate the future sensibly." Emotionally he finds the institution children very primitive. They indiscriminately demanded affection and attention, and yet could form no permanent ties; not being able to feel for other humans, they were not upset by hostility or cruelty to others.

Goldfarb considered that the deprivation in infancy associated with institutionalisation results in a basic defect of the total personality. It is as if the institution child personality "is congealed at a level of extreme immaturity." He cannot be taught as readily as other children because of deficiency in attention and lack of capacity to grasp ideas. "He has little self-insight, and direct treatment is commonly ineffective, particularly at the adolescent level."

Goldfarb claims that "one would hardly describe the institution regimen as brutal or aggressive. Its major defect lies in the bare and narrow horizons of experience it offers. This last applies both to the world of things and to the world of people. The institution child thus establishes no specific identifications, and engages in no meaningful relationships with other people. The basic motivations to normal maturation and differentiation of personality are absent." All this seems to be a terrible indictment of the effects of institutionalisation. You will notice the stress laid on the catastrophic effect of a rigid environment. But very little reference is made to the kind of child who has been exposed to these special environmental conditions.

Apart from these American studies, what confirmation can be found for this concept of the "institution child?"

In this country we have had the advantage of the masterly studies of Miss Anna Freud and Miss Burlingham at the Hampstead Nursery. They published clinical reports but no statistics. They pointed out that residential nurseries provide excellent conditions for the development of motor skill and early social responses, but have limitations which hamper emotional development and the formation of character. This character formation, this establishment of personal values, depends largely on the strength and depth of the personal attachments which give rise to them. If the child has no loving adult to identify with, it will fail to develop values and standards of its own.

In the residential nursery, if the grown-ups remain remote and impersonal, or change often, so that no permanent attachment is possible, then Miss Freud suggests that institutional education will fail to develop moral standards.

Nevertheless, in their report, there are numerous examples of personal relationships developing between child and nurse, and between child and child—relationships which were obviously of considerable depth, judging by the reactions which occurred when separation was inevitable. The institution child is not necessarily affectionless. I mention this matter of affectionless character, as Dr. Bowlby lays great stress on it, and claims that children showing it have a remarkably distinctive history of prolonged separation from their mothers or foster mothers; he considers them unusually clear examples of the distorting influence of a bad early environment. But he lays stress on the separation from the parent. I would ask why was it necessary to separate the child from his home. One of Dr. Bowlby's cases had a schizophrenic heredity, and he had *not* been separated from his mother. But on examination of his detailed studies it appears that of the 11 affectionless children about whom something was known of the parents, nine had an unstable, violent, alcoholic, or antisocial parent.

So much for the background to our own investigation. In this the field work was carried out by Miss Sykes, psychiatric social worker and Miss MacKinlay, educational psychologist, to whom I am deeply grateful for their thorough and painstaking studies, often carried out under great difficulty.

The questions we set ourselves to answer were: are there any differences in educational attainment between a child brought up in an institution, and a child brought up in his own home?

Does the child brought up in an institution show any difference in social maturity from the child reared in his own family?

Does the institution child shew any special difficulty in adapting himself to society when he leaves the shelter of the institution? Can the institution child make friends? Does he find it easy to adapt himself to conditions of work?

The survey began with an investigation of the institution child in the institution during the year of school-leaving age. The social worker visited the institution and contacted the staff; the educational psychologist interviewed the child and administered a battery of tests.

Six months to a year later, when the child had left the institution, the social worker visited the foster home or lodging and interviewed the child and tested social maturity, using the Vineland Social Maturity Test. She also interviewed, where available, foster parents and employers to get a comprehensive picture of the child's adaptation.

The controls were a group of senior school children brought up in their own homes, who underwent exactly similar investigations.

I do not propose to consider in detail all the results of this investigation. It is hoped that the National Association of Mental Health who sponsored the investigation, with the welcome help of the Nuffield Hospitals Trust, will publish our results in detail.

But I wish to confine myself to one general aspect of our findings.

On comparing the 50 institution children with the school control group of 52, we found that the average social quotient of the institution child was 92.9 per cent. compared with the control groups' average of 106.5 per cent.—a difference of 13.6 per cent.

It might be thought that here is confirmation of the handicap to which children brought up in institutions are subjected.

But when we studied the reasons for which the children had been placed in the institutions visited, we were struck by the fact that only just over a quarter of our sample were orphans. Another quarter had been institutionalised because one or both parents had been admitted to mental hospitals or colonies for mental defectives.

The high proportion of mentally unstable parents invited comparison with the control group. We considered factors which might have a constitutional or hereditary basis, such as insanity, mental deficiency and epilepsy, and also took into account authentic reports of bigamy, incest, family desertion necessitating action on the part of the authorities, terms of service in prison or approved schools or habitual promiscuity. Relatives for this purpose were restricted to parents and sibs, as in the case of institution children, records in the files of public assistance offices rarely had information about other members of the family.

When, therefore, these institution children with insane, defective, epileptic and antisocial relatives were grouped together, we found that they constituted 74.3 per cent. of the total; in comparison with 11.5 per cent. of the school control group.

This high proportion of institutional children (nearly $\frac{3}{4}$) with possible hereditary handicaps, suggested a further comparison.

The whole material of institution children and controls was regrouped, into those children with epileptic, insane, defective and antisocial relatives, and those children whose family record was clear of these taints, and their social quotients compared.

The average social quotient of the children with unsatisfactory family records was 91.6 per cent. compared with the presumed normal children whose social quotients averaged 105 per cent.

The difference of 13.4 per cent. is exactly the same as when institution children were compared with normal controls.

That is to say, the same degree of social retardation is to be observed whether the children are grouped according to environmental circumstances (home or institution) or classified according to hereditary factors (unsatisfactory or satisfactory parents).

Such a finding certainly weakens the case of those protagonists who argue that any social or personal retardation is attributable exclusively or mainly to environmental influences.

This finding sent me back to a study of the original American papers on the institution child. A study of Lowrey's 1940 paper shewed that of his 28 cases only 16 had intelligence tests reported. But one was feeble-minded, 10 had I.Q.'s under 90. Further, of possible hereditary factors, case 1 had a neurotic "lowgrade" mother, case 2 a dull unstable mother and a father

with a criminal record ; case 5 had a delinquent moron for a father, and a dull and unstable mother ; case 6 had a schizophrenic mother ; case 8 had a paranoid mother ; case 9 had a schizophrenic mother. Briefly, two-thirds of the cases reported at length by Lowrey had parents of inadequate, unstable or psychotic mentality.

A study of Goldfarb's series also revealed a discrepancy of a very considerable nature in intelligence.

In his comparable study of adolescents the average I.Q. of his institution group was only 72 per cent., compared with his control group of 95 per cent. And one cannot avoid the conclusion that many of the unfavourable features of his so-called institution type are really attributable to borderline defect rather than to institutionalisation as such.

It would only be natural that the authorities would board-out their brighter children, as more acceptable to potential foster parents, and be forced to retain the dull and near-defectives.

Goldfarb claimed that the institution children in his group were singularly unable to form abstract concepts, and failed conspicuously in tests involving conceptual performance. But this is only to be expected in a group of borderline defectives.

In our present series an attempt was deliberately made to find controls of a corresponding intellectual level. Miss Mackinlay found the average I.Q. of our institution children 90 per cent. compared with the average of the control group 99.5 per cent. Both figures therefore fall within the average range of intelligence. Our findings therefore suggest that constitutional factors are at least as important as environmental factors in subsequent social maturation.

I think our studies therefore confirm the claims of Doll, who maintains that there are probably limits to the unfolding of the social personality, just as there are limits to the development of intelligence.

The influence of training and environment is principally effective during the period of development. It is ineffective after social maturation is complete. This, if true, has important bearings in the institutionalisation of children, particularly defectives, as Doll has found that the rate of social maturation slows down after 15 in the feeble-minded compared with normal development until the 25th year.

Doll has investigated a series of families using his social maturity test, and has demonstrated that social maturity appears to be distributed in similar fashion to intelligence. He prints genealogical trees of four generations, shewing that in some families the social maturity never reaches a normal level, while in other families the social maturity is always above average.

Doll was inclined to believe that social capacity was very largely an innate factor, and only slightly modified by environment, though he admitted that foster-home placement capitalises social competence to better advantage than does institutional care.

Now the Slaters in discussing the various theories which may be advanced to account for the phenomena of the neuroses and maladjustment, favour that group of theories which considers that the constitutional basis is in part

hereditary, but may be due to several factors, with dissimilar effects which may overlap.

They propose the theory that a very large number of characteristics can be differentiated amongst men, each of which plays a part in determining the success with which the individual adapts to circumstances.

"The normal man possesses certain characteristics that promote success, and lacks others in roughly equal proportions.

"But the man with a tendency to maladjustment lacks many characteristics that promote success and possesses few.

"In other words, every individual possesses characteristics, variable in strength, which render him more or less liable to maladjustment. Whether he succumbs or not depends on the extent to which he is endowed with qualities which help to make him less vulnerable to breakdown, and on the nature and degree of the stresses to which he is exposed."

If I may add an analogy. In the parable of the Sower, both seed and soil were taken into account. Not only may the seed fall by the wayside, on stony places, amongst thorns, or on to good ground; but even the seed with good environment had different productive capacity, the best a hundredfold, some sixtyfold, some only thirtyfold.

And was it not the same Thinker who asked, "Do men gather grapes of thistles, or figs from thorns?" Of course the question is not a simple one to answer.

Indeed Kanner warns us:

"We must especially guard ourselves against any sort of formulations calling for an exact statement expressed in percentages, as to how much a child's behaviour disorder is constitutional and how much environmentally determined. It is not our desire to separate things which are so thoroughly fused and integrated that they cannot be separated, or to draw lines which cannot be drawn even approximately or artificially."

One of the main difficulties, of course, is that normally the unstable, psychotic, defective or social parents not only may be the source of the child's constitutional make-up, but also constitute the main personal influence in the child's environment, particularly if it is the mother. And as these handicapped parents are themselves maladjusted, the environment of their children teems with stresses and tensions to which the normal child is not exposed. One only has to consider the effects on an adolescent boy of an alcoholic father who comes home violent and quarrelsome and turns his wife and family into the street in the middle of the night. A severe stress for a normal boy; but for one who may already inherit psychopathic tendencies—a catastrophic stress.

Or, again, consider the example of the unfortunate boy of 12 whose mother was sent to prison for manslaughter after performing an illegal operation—again a situation involving domestic tensions and conflicts almost beyond the capacity of an inherently stable boy to endure.

Michael Fordham has discussed the *participation mystique* of the young child with his parents, and stressed the burdens that are laid on the young child by neurotic parents; and Wellisch has stressed how completely identified with his parents' psyche is the child during the first years of his life. It is interesting to note that in Wellisch's case of *folie à deux* in mother and son, the son's depression improved when he was separated from his mother.

Lowrey claimed that early separation from the mother was the factor in determining the institutional type of character, and suggested that the critical age was two years.

But my own experience of some of these psychopathic, deranged and defective mothers would suggest that early separation of mother and child would be an advantage to the child. There was the adolescent girl with a psychopathic mother, who miserably exclaimed—"If I didn't have parents, I'd be an orphan, but I'd know who *I* was anyway. If you live in a choked up adult world, how can you know anything? You're lost. They—the adults—can be sure of me—I can't be sure of them!"

Actually, we investigated this question of age of institutionalisation in our own series, and we were unable to confirm Lowrey's claim. Of 16 children admitted to institutions before the age of two, the social quotient on leaving school age was 93.1 per cent. compared with an average social quotient of 92.8 per cent. of 34 children admitted to institutions after the age of two. The difference of 0.3 per cent., of course, is not significant. Our studies therefore suggest that in this country the institution child is not a clinical entity. In many cases the reasons for his institutionalisation are the rejecting attitudes of his unstable, psychopathic, defective or psychotic parents. Inheriting in part some of their handicaps he is the more *vulnerable* to the stresses of separation anxiety and the deprivation of personal relationships. But when, as often occurs, he is also dull and backward in intelligence, these experiences are not indelible, their effects are fleeting and soon forgotten, and the father or mother becomes a mythical figure bearing no more significance than the King or the Prime Minister, as far as his personal life is concerned. The important persons in his life are the matron and her assistants and the group of children with whom he lives.

If these findings are generally true, it means that the average institution child because of his inherited defects, in social capacity and also perhaps in intelligence requires more individual care and understanding than the average child secured in his own family.

And this finding gives force to the recommendation of the Curtis Committee, that the small group home should contain not more than 12 children.

I know I shall be accused of a Calvinistic bias in proposing this psychology of predestination. But have we not already accepted the implications of such a psychology for our mental defectives, and are we not pressing for measures to provide a suitable environment for their limited intelligences?

It is not illogical to believe that we will be forced to take the same steps for our social defectives. The tragedy of these children is that in the past and even in the present we have placed, and are placing, these already handicapped children in an environment which has tended to accentuate their shortcomings—to highlight their limitations.

Afraid of society, do they not visualise it as that hard man reaping where he has not sown, gathering where he has not strawed, and wrapping his single talent in the napkin of respectability, and burying it in the ground? Surely that impoverishment of society is a greater risk even than the delinquency which tends to attract all our attention?

But the finding that constitutional factors are relatively so important need not depress us unduly. As Dr. Carroll has said, "If we cannot effect real changes in character, it should be possible to alter the pattern of behaviour in which that character is expressed."

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ELECTRO-NARCOSIS IN THE TREATMENT OF SCHIZOPHRENIA.*

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I CARRIED out 2,443 treatments by electro-narcosis on 152 patients, between 29 January, 1948, and 19 February, 1949, without fatality, and without any adverse personality change attributable to the treatment. Of these patients 105 were schizophrenics, whose treatment was completed before 29 January, 1949. This series alone is considered in detail here, but the experience gained from the treatment of the remaining patients is taken into account, especially in relation to difficulties and dangers.

TECHNIQUE.

I used the Shotter-Rich electro-narcosis apparatus, and the basic technique described by Paterson and Milligan (1947), Paterson (1948*a* and 1948*b*), and Milligan (1948). Reference was also made to the following American workers, who used a somewhat different apparatus, but a similar basic technique: Frostig *et al.* (1944), Tietz *et al.* (1946) and Tietz (1947). There is no need to repeat what these authors have written, but the following technical points were stressed in the present series:

1. The standard of physical fitness required was the same as for electrical convulsion therapy without curarization.

2. Unless curare was used, or difficulties were anticipated, treatment was carried out by one doctor. It was therefore considered essential to have a good nursing team, each member being trained to report instantly any significant change in the patient's condition. The patient's pulse rate and volume were kept under constant observation.

3. The "Glissando" technique, described by Tietz (1947) and Paterson (1948*a*), was always used.

4. The experience gained from the treatment of the first forty cases led me to use preliminary thiopentone anaesthesia in all subsequent cases. Intravenous administration was the usual method, but in the few cases where this was impossible, rectal thiopentone supplemented by a small inhalation of ethyl chloride proved satisfactory. The use of thiopentone ensured amnesia for the period of treatment and diminished the violence of muscular contraction, especially as regards flexion of the spine. Protection by curarization was therefore rarely necessary and was used in only four cases in this series. When thiopentone was used I considered it important to elicit the characteristic signs of electro-narcosis, namely, flexion of the arms and inspiratory stridor, in order to be sure that an adequate dose of electricity was being administered.

5. Tietz *et al.* (1946) indicated that placing the electrodes in a forward position had an effect similar to that produced by using a relatively small dose of electricity, while a rearward position corresponded to an increased dose.

* Abstract of a thesis accepted for the degree of M.D. of the University of Edinburgh.

Following this hint I adopted the practice of starting treatment with the electrodes placed frontally, and then moving them back when breathing was fully established. This manoeuvre made control more rapid and flexible. Used in conjunction with thiopentone anaesthesia, it abolished convulsive phenomena in a large proportion of cases.

6. After treating about fifty cases I made a habit of starting each patient on a short treatment of $1\frac{1}{2}$ to 2 minutes and lengthening the time on subsequent occasions in the light of the patient's reactions, to a maximum of seven minutes.

7. The number of treatments given to each patient varied according to progress, the shortest course consisting of three treatments, the longest of forty-one. Electro-narcosis was normally carried out three times a week. Many schizophrenics who showed little change after twelve treatments did well on longer courses.

In conclusion, I would emphasize that once the technical advantages of thiopentone anaesthesia, electrode movement and gradual lengthening of the treatment period were appreciated, electro-narcosis without them appeared barbarous and unjustifiable.

DIFFICULTIES AND DANGERS.

These were described and discussed by Garmany and Early (1948). Special attention was therefore paid to the points made by these authors, and the following account deals with untoward events in all 156 patients treated.

1. Cardiovascular shock occurred in one case, subsequently found to be suffering from very early pulmonary tuberculosis which had eluded discovery by physical examination. Her condition was not serious enough to cause alarm and recovery was complete in 48 hours.

2. A reactivation of the psychosis with excitement, hallucinosis and confusion occurred in 15 per cent. of cases prior to the introduction of thiopentone. In two cases this was followed by striking improvement, which had not occurred before. In no case was the patient worse after such an episode than before. In all cases the condition cleared up in periods varying from three days to three weeks. After the introduction of thiopentone this sequel was rather less frequent and no more serious in its effects.

3. Before the introduction of thiopentone, some memory of the initial shock was present in 15 per cent. of cases. Memory of a substantial part of the treatment occurred in 6 per cent., but in only one case was there serious fear of a repetition of the experience. This patient was later given a full course satisfactorily with thiopentone. After the introduction of thiopentone, this complication ceased to exist.

4. Treatment was cut short in several cases owing to weak or irregular cardiac action during treatment. All were known to have cardiovascular abnormality before treatment was started. This difficulty was therefore largely due to the acceptance of greater risks with increasing experience.

5. A fracture of the right articular process of the eighth dorsal vertebra occurred in one man, and muscular injury in two, before the introduction of thiopentone. No serious injuries occurred subsequently.

6. Four cases showed sensitivity to thiopentone itself.

7. A large swelling of the thyroid gland of sudden onset and unknown causation occurred in one woman. It subsided in ten days without ill effect.

8. Four patients refused further treatment as they felt apprehensive, even though they had been given thiopentone. Memory of the treatment could not be elicited. All were hyperanxious types liable to become apprehensive of anything, even on flimsy grounds.

9. Small burns of the forehead occurred in several cases while the electrodes were new and the plating intact. When the plating wore off the burns ceased. Removal of the plating on new electrodes prevented the occurrence of further burns.

10. One patient who had previously undergone leucotomy showed rapidity and irregularity of cardiac action at an unusually low dosage level of electricity. When this was recognized and allowed for, further treatment proceeded smoothly.

ANALYSIS OF RESULTS.

Before starting electro-narcosis, a survey was made of all cases of schizophrenia admitted to Barming Heath Hospital during a ten-year period before the introduction of shock therapy for schizophrenia. These cases had all been assessed by myself, or by one or other of two psychiatrists whom I knew well, so any personal bias operated similarly on control and treated cases. Schizophrenics transferred to other hospitals within a year of admission were excluded from the controls, as continuity of personal observation was lost. As the reason for transfer was place of residence, they presumably constituted a random sample, whose elimination had no statistical significance. Schizophrenics who died within a year of admission were also excluded, to counterbalance the fact that patients in poor physical condition were not lightly accepted for electro-narcosis. All other patients regarded as schizophrenics were included in the control series.

The exact delimitation of the boundaries of the control group was a considerable problem. In drawing a line between paranoid schizophrenia and predominantly paranoid conditions, reliance was frankly placed on personal judgment to ensure that it was drawn in the same place in the control and the treated series. It is true that, for example, affective failure, incongruous emotional responses, silly mannerisms, vagueness of thought content and impulsiveness were regarded as criteria of schizophrenia. Resentment and relative preservation of the personality were taken as indications of predominantly paranoid states. However, as these points were capable of different interpretations by different psychiatrists, it was felt that reliance on personal judgment could not be evaded. The continuity of personal viewpoint was also used to eliminate schizophrenic reactions and atypical affective disorders. In addition, all patients were eliminated from the control series who were admitted to hospital three times in the ten-year period, and achieved remission or social recovery on each occasion. The results in the control series were derived from assessment of the clinical state of the patients one year after admission.

The control series consisted of 557 patients, of whom 295 were men and 262 were women. Twenty-three patients had two attacks within the ten-year period,

so the total number of "attacks" considered was 580; 137 of the patients had had other attacks before the start of the ten-year period. The patients in the control series received all the benefits of hospital treatment accorded to the electro-narcosis cases, with the single exception of electro-narcosis itself. The results were classified in the following five categories:

1. *Complete remission*.—These patients were free from psychotic symptoms when they left hospital, but had not necessarily achieved insight. This standard was therefore lower than the "Grade A" of Tietz *et al.* (1946).

2. *Social recovery*.—These patients had left hospital with residual symptoms insufficiently severe to prevent them from doing useful work and adjusting to some degree to domestic life. Cases removed from hospital to be cared for at home were not included.

3. *Improved*.—These patients were relieved from their symptoms to some extent, but not sufficiently for the hospital to initiate their discharge.

4. *Not improved*.—This group included those who were unchanged or worse than on admission.

5. *Relapsed*.—This class consisted of patients who were readmitted after achieving complete remission or social recovery.

The important figures obtained were as follows:

I. The results at one year of all attacks—

Category.	Number of patients.	Percentage.
1	63	10.9
2	141	24.3
3	116	20.0
4	247	42.6
5	13	2.2
	580	100.0

2. The results at one year, related to the duration of illness before treatment. Admission to hospital was regarded as the beginning of treatment. Patients were divided into six duration groups:

- (1) Three months or less.
- (2) Over 3, but not more than 6 months.
- (3) Over 6, but not more than 12 months.
- (4) More than one year, but not more than 2 years.
- (5) More than 2 years, but not more than 3 years.
- (6) Over 3 years.

Category.	Duration Groups.					
	1.	2.	3.	4.	5.	6.
1	46	7	6	4	0	0
2	81	19	12	17	1	12
3	37	10	20	16	9	24
4	65	31	33	36	24	57
5	8	2	1	0	1	1
	237	69	72	73	35	94

Expressed as percentages these figures read :

Category.	Duration groups.					
	1.	2.	3.	4.	5.	6.
1	19.4	10.2	8.3	5.5	0.0	0.0
2	34.2	27.5	16.7	23.3	2.9	12.8
3	15.6	14.5	27.8	21.0	25.6	25.5
4	27.4	44.9	45.8	49.3	68.6	60.6
5	3.4	2.9	1.4	0.0	2.9	0.1

3. Average stay in hospital : The average period spent in hospital by those patients who achieved categories 1 and 2 was 28 weeks.

4. Average duration before relapse : The average period between the dates of the first and second admissions in relapsing cases was 1 year and 11 months.

The rise in the social recovery rate in the group ill for more than three years requires explanation. Many of these patients had been ill for many years with few acute symptoms. They were tolerated by relatives until an untoward incident or unpleasant personal habits made admission necessary. As soon as the crisis was over, or improvement of any kind occurred, the relatives pressed for their discharge. As most went out to resume menial farm duties, they were given the benefit of the doubt and classified in Category 2.

RESULTS ACHIEVED WITH ELECTRO-NARCOSIS.

In the year starting on 29 January, 1948, the treatment of 105 schizophrenic patients with the help of electro-narcosis was completed ; 21 other patients were considered to be schizophrenics, and electro-narcosis was contemplated in their cases, but rapid spontaneous improvement occurred, so shock therapy was felt to be unjustifiable. Although not considered in detail, these patients had a bearing on the assessment of the results of electro-narcosis.

As many of the patients treated were cases of long standing, with a very poor prognosis, a direct comparison of the overall results in the electro-narcosis series, with the results at one year of all the control cases, was felt to be misleading. Allowance was, therefore made for the duration of illness before treatment, this being reckoned up to the start of electro-narcosis in the electro-narcosis series.

The method of comparison was as follows :

The 105 electro-narcosis cases were distributed as follows in duration groups :

Group.					
1.	2.	3.	4.	5.	6.
15	11	14	21	20	24

Taking Group 1 first : The expected results in 100 cases in Group 1 were known to be as follows:

Category.				
1.	2.	3.	4.	5.
19.4	34.2	15.6	27.4	3.4

The results to be expected in 15 cases were therefore these figures multiplied by 15 and divided by 100, namely—

Category.				
1.	2.	3.	4.	5.
2.91	5.13	2.34	4.11	0.51

After dealing with the other duration groups in the same way and adding the numbers falling in each category, the results were :

Category.				
1.	2.	3.	4.	5.
6.34	19.03	23.66	54.06	1.86
or 6	19	24	54	2

if expressed to the nearest integer.

These figures indicated the expected distribution in categories of the 105 patients treated, if the results were the same as in the control series.

Expressed as percentages these figures became :

Category.				
1.	2.	3.	4.	5.
5.7	18.1	22.8	51.5	1.9

Of the patients treated the numbers falling in the various categories were as follows :

Category.				
1.	2.	3.	4.	5.
15	28	20	39	3
or 14.3	26.7	19.0	37.1	2.9

For ease of comparison these figures can be tabulated together :

	Category.				
	1.	2.	3.	4.	5.
Controls . . .	5.7 .	18.1 .	22.8 .	51.5 .	1.9
Treated cases . .	14.3% .	26.7% .	19.0% .	37.1% .	2.9%

The expected discharge rate (Categories 1 and 2), calculated from the control group, was 23.8 per cent. The discharge rate actually achieved was 41.0 per cent.

Of the patients discharged after electro-narcosis, 17, or 39.5 per cent., had been ill for more than a year when treatment was started.

The average period from the start of electro-narcosis until discharge was 15 weeks.

In assessing these results, attention was paid to the 21 cases of schizophrenia admitted during the year in which electro-narcosis was used, but not given

shock therapy owing to the rapidity of their progress without it. Some doubt was felt as to whether 6 of these cases were strictly comparable to the control group, so the remaining 15 only were considered. It was felt that cases making rapid progress were present in the control series, but excluded from the electro-narcosis group. As these cases all left hospital, a factor raising the discharge rate in the control group, relative to the electro-narcosis group was felt to be present. It was impossible to assess how many patients in the control group improved too rapidly for hypothetical treatment by electro-narcosis, so an attempt was made to assess the importance of the issue by indirect means.

Supposing, for the sake of argument, that these 15 patients had been given electro-narcosis and that their remissions or social recoveries had been attributed to the treatment, what would the result have been? The total series would have consisted of 120 cases. The actual results achieved, and the expected results derived from the control series, expressed as percentages and compared in the manner already described would have read as follows:

		Category.				
		1.	2.	3.	4.	5.
Controls	.	7.5	19.2	22.5	49.2	1.6
Treated cases	.	19.1	29.2	16.7	32.5	2.5

The ratio of actual results to controls in categories in this hypothetical series was 48.3 : 26.7, or 180 : 100.

The ratio of actual results to controls 1 and 2 in the real series of 105 cases was 41.0 : 23.8, or 172 : 100.

The results in the hypothetical series were better than those in the real series in the proportion of 180 : 172 or 104.5 : 100.

The fact that these 15 cases did not appear on the credit side of the electro-narcosis account had the effect of making the control series read approximately 4½ per cent. too high in relation to the series treated by electro-narcosis. As it was no part of my programme to strain figures to the utmost to gain an effect, this fact was ignored in the final comparisons of control and treated cases.

In order to check the results more closely, assessments were made of the figures at earlier points in the series. At the time this survey was completed, 10 months had elapsed since electro-narcosis was finished in the first 43 cases; 6 months had passed since the end of electro-narcosis in the first 69 cases. Assessments were therefore made at these points.

The results in the first 43 cases were:

		Category.				
		1.	2.	3.	4.	5.
Controls	.	4.7	16.2	23.3	53.5	2.3
Treated cases	.	18.6	20.9	11.7	46.5	2.3

Forty-seven per cent. of those in categories 1 and 2 had been ill for more than one year.

The results in the first 69 cases were :

	Category.				
	1.	2.	3.	4.	5.
Controls . . .	5.8	17.4	23.2	52.2	1.4
Treated cases . .	17.4	24.6	17.4	37.7	2.9

44.8 per cent. of those in Categories 1 and 2 had been ill for more than one year.

The ratio between treated and control cases was therefore similar at three points in the series.

DISCUSSION OF RESULTS.

Any method of comparing groups of cases of uncertain aetiology and protean clinical manifestations is open to objection. When the disorder in question affects the total personality, comparison is made doubly difficult. I therefore tried simply to be as fair as possible, without attempting mathematical accuracy.

Petrie and Sands (1948) discussed the difficulty of assessing the results of shock therapy in depressive cases. They cited Penrose (1946) as having satisfied himself by statistical enquiry that electrical convulsive therapy held no advantage over less violent procedures when a long range was taken, with a minimum of five years since treatment as a standard. They went on to say that although they hesitated to question the purely statistical validity of the finding, they felt it necessary to point out that there was little agreement between this view and the results seen day by day in hospital wards. They thus implied the existence of a cleavage between those who rely on statistics in assessing results, and those who rely on clinical judgment. Indeed, it would probably be fair to say that most psychiatrists, in using shock therapy, are backing their clinical judgment rather than relying on statistical evidence.

The difficulty facing the statistician dealing with schizophrenia lies in the absence of demonstrable aetiological factors or measurable clinical manifestations of a kind known to be significant. Academic psychologists agree about the difficulty of defining what is meant by a trait, let alone the assessment of the significance of different traits. Clinical psychiatrists do not deal with objectively demonstrable facts, but with observations and judgments coloured by the experience of the observer, and probably by his temperament. Further, it is generally agreed that the measurement of the dimensions of personality is in its infancy. Therefore, in attempting to assess the results of any form of treatment with statistical accuracy, the opportunities for false quantification are almost infinite.

I therefore attempted to use statistics simply to give more precise expression to clinical findings, and tried to prevent statistics taking leave of reality by constant reference back to the clinical foundation on which they were based.

To ensure reasonable fairness of comparison, care was taken to see that all cases in the control and treated groups fell within the same descriptive limits. All cases admitted during the period of survey were treated, except those physically unfit and those who made rapid spontaneous progress. In addition,

a number of patients previously admitted but making no progress with ordinary hospital care were also treated. It is clear, therefore, that no effort was made to choose for treatment a series of cases of better inherent prognosis than the controls.

The importance of the duration of illness before treatment in relation to the outcome in schizophrenia has often been stressed in the literature on insulin therapy. Muller (1937) claimed 73·8 per cent. of recoveries in patients who had been ill for less than six months, 63·3 per cent. in patients who had been ill for less than a year, 37·8 per cent. in those treated before the end of two years, and 15·4 per cent. in those of more than two years' duration. Ross and Malzberg (1939) claimed a recovery rate of 26·1 per cent. in cases who had been ill for less than a month. This fell to 2·1 per cent. in those with a duration of 11 to 14 years. Sargant and Slater (1948) strongly emphasized the importance of the duration of illness in choosing cases likely to respond to insulin therapy. It was therefore interesting to find the same trend reflected in the survey of the control group for the present series.

From the viewpoint of duration of illness before treatment, the electro-narcosis group was prognostically much less favourable than the control group. The percentage of cases in the duration groups described above was as follows :

		Duration Group.					
		1.	2.	3.	4.	5.	6.
Controls	.	40·9	11·9	12·5	12·5	6·0	16·2
Electro-narcosis							
cases		14·4	10·5	13·3	20·0	19·0	22·8

Nevertheless, an overall comparison of the results in control and electro-narcosis cases showed a greater proportion of discharges in the latter, the actual figures being respectively 35·2 per cent. and 41·0 per cent.

Confirmation of the fairness of the method of comparison used was obtained when the 15 untreated cases were considered in relation to the 105 treated cases. In a direct comparison of the over-all results in both series, the addition of these 15 cases would have improved the treated series by 14 per cent. in relation to the controls. However, as the 15 cases were almost all of short duration, the adjusted result showed an increase of only $4\frac{1}{2}$ per cent. over the controls, a remarkable absorption of a heavy and unfair load.

The fact that 39·5 per cent. of patients discharged after treatment by electro-narcosis had been ill for more than a year, indicated that the treatment did not merely pick out those of inherently good prognosis from an otherwise unfavourable group. The average stay in hospital after the start of electro-narcosis was 15 weeks, compared with an average stay in the control series of 28 weeks. Allowing 4 weeks for investigation and evaluation of cases before giving electro-narcosis, this represents a saving of two months in hospital for each patient.

To summarize, the short-term results of electro-narcosis showed a ratio of discharges in treated cases to discharges in the control series of the order of 5 : 3. A comprehensive recent study of the long-term results of

insulin therapy was published in the New York State Hospitals' Report (1944), cited by Sargant and Slater (1948). A series of treated cases was compared with a series of untreated cases of similar type and prognosis. Of the treated cases 80 per cent. were discharged, while of the untreated cases 59 per cent. were discharged, making the ratio between discharges in the two groups approximately 4:3.

As the figures for the present series represent short-term results I do not wish to strain comparison too far. Relapses in the cases treated by electro-narcosis will undoubtedly occur. In the control series, the average period between admissions in relapsing cases was 1 year and 11 months, with a wide scatter about that mean. Therefore a five year study at least will be required to estimate the long-term value of electro-narcosis. The short-term results, however, bear comparison with those from insulin therapy.

No detailed comparison was made of the results in schizophrenia of electro-shock and electro-narcosis. However, the first twelve electro-narcosis patients had all had electro-shock, without lasting benefit. After electro-narcosis, four achieved complete remission, and one social recovery.

CONCLUSIONS.

I do not suggest that electro-narcosis is a rival to insulin shock therapy, or liable to supersede it. I submit, however, that if insulin is not available, electro-narcosis is an equally safe alternative, which may yet prove to be in the same class. I suggest that a thorough investigation of the long-term results of electro-narcosis is both justifiable and desirable, especially in view of the contention of Sargant and Slater (1948), that the main drawback to insulin therapy is the difficulty in providing it at once for all schizophrenics coming under observation. Such an enquiry might deal with the type of case especially suitable for each method. In this connection I formed the clinical impression that the affective component of schizophrenia responded principally to electro-narcosis. It may be, therefore, that some patients, especially simple schizophrenics, may respond to electro-narcosis although resistant to insulin therapy.

I submit, therefore, that a preliminary case has been made out to show that, in present conditions, electro-narcosis has a useful place in the treatment of schizophrenia.

SUMMARY.

1. An account is given of the administration of 2,443 treatments by electro-narcosis to 152 patients, with special reference to the treatment of 105 cases of schizophrenia.

2. Points of technique found by experience to be especially important are emphasized.

3. The difficulties and dangers encountered are described.

4. A description of a survey of 559 cases of schizophrenia admitted to hospital during 10 years prior to the introduction of shock therapy is given for purposes of control.

5. The difficulties involved in comparing two groups of schizophrenics are discussed, and the reasons for the method chosen are given.

6. The results achieved after the use of electro-narcosis are compared with the control group in a manner which contrasts groups of cases of similar duration of illness before treatment.

7. The electro-narcosis group is shown to be of intrinsically worse prognosis than the control group, as regards duration of illness before treatment. Yet the percentage of discharges after electro-narcosis is shown to be greater.

8. Comparison of groups of similar duration of illness shows that the ratio of discharges after electro-narcosis to discharges in the control group is approximately 5 : 3.

9. It is emphasized that electro-narcosis should not be regarded as a rival or possible successor to insulin shock treatment.

10. It is submitted that electro-narcosis has a useful place in the treatment of schizophrenia, and that it is justifiable and desirable to undertake a survey of the long-term results of the treatment.

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THE TREATMENT OF MENTAL DEFECTIVES WITH ANEURIN FOR ONE YEAR.

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IN a previous article (Rudolf, 1949) an account was given of the results of treatment of 90 defectives with 3 mgms. of aneurin daily for a period of six months. The patients had been resident in Hortham Colony for periods of from 3 to 17 years. None had shown any improvement for at least one year prior to the beginning of the treatment.

The present article deals with the treatment of 41 of the cases for a period of one year. All these patients, at the end of six months' treatment, showed improvement in one or more of the four aspects of behaviour in the lodge, behaviour at school or work, social age or intelligence quotient. Details of the selection and types of cases, methods of observation, types of tests used, etc., will be found in the article to which reference has already been made.

Results are seen in Table I, which shows that 24 cases improved at the end of both the first and the second six months of treatment in behaviour in the lodge, at work, in social age or in intelligence quotient.

Improvement in the first six months did not continue during the second six months in the same subject in 17 cases.

The patients who improved in their lodge or in their work by the ends of both the first and second periods of six months changed as below :—

No. 8.—At end of first period was taking more interest in her surroundings; by the end of the second, was able to sit up.

No. 12.—At end of first period was taking more interest in his surroundings; by the end of the second, was moving more freely and more actively.

No. 35.—Improved in his reading by the end of the first period, being able to read 3-lettered words. At the end of the second period he could read words of 4 letters, had learned to multiply and to give change. In the lodge, general behaviour had improved and he was less restless.

No. 36.—At the end of the first period he had improved in his talking and was taking a greater interest in Montessori apparatus. This improvement continued during the second period.

No. 39.—In the first period, improvement occurred in both reading and arithmetic. At the end of the second period, he could add without the help of counters, necessary at the end of the first period.

No. 42.—At the end of the first period, he had become more contented, less noisy although speaking more, and was taking a greater interest in his surroundings. At the end of the second six months he was more active. He now used a duster and a floor polisher and chased others in play, something he had never previously done.

No. 48.—He was happier, less boisterous and his tempers were decreasing at the end of the first six months. Slight improvement had taken place in his work. By the end of the year, no further evidence of impulsiveness or hot temper had

TABLE I.—*Improvements in the lodge, at work and in tests of cases treated for one year, at six monthly and 12 monthly intervals*

Patient's No.	Lodge		Work		S.A.		I.Q.	
	6 mos.	12 mos.	6 mos.	12 mos.	6 mos.	12 mos.	6 mos.	12 mos.
8	..	+	+	0	0	—	+	—
10	..	+	—	0	0	—	—	—
12	..	+	+	0	0	—	—	—
16	..	+	—	0	0	—	—	—
20	..	+	—	0	0	—	—	—
25	..	—	—	—	+	+	—	—
27	..	—	—	—	+	+	—	—
28	..	—	—	0	0	+	—	—
29	..	—	—	0	0	+	+	—
33	..	—	—	—	+	+	—	—
35	..	—	+	+	—	+	+	+
36	..	—	—	+	+	+	—	+
39	..	—	—	+	+	—	+	+
40	..	—	—	—	+	+	—	+
41	..	—	—	—	+	+	—	—
42	..	+	+	+	+	+	—	—
44	..	—	—	—	+	—	+	—
45	..	—	—	—	+	—	—	+
46	..	—	+	—	+	+	—	—
47	..	—	+	—	+	—	+	—
48	..	+	+	+	—	+	—	+
49	..	—	—	—	+	+	—	—
50	..	—	—	—	+	+	+	+
51	..	+	+	+	0	+	+	0
55	..	—	—	—	—	+	+	—
56	..	—	—	0	0	+	+	0
60	..	—	—	—	—	—	+	+
62	..	+	—	+	—	+	+	—
63	..	—	—	—	—	+	—	+
65	..	—	—	—	—	—	+	—
66	..	+	—	+	—	+	+	+
68	..	—	—	—	+	+	+	—
73	..	—	—	0	0	—	+	+
74	..	—	—	—	—	+	+	+
76	..	—	—	+	—	—	+	+
77	..	—	—	—	—	+	—	+
79	..	—	—	—	—	+	—	—
80	..	+	—	—	—	—	—	—
86	..	—	—	—	—	—	+	—
87	..	+	—	+	0	+	—	+
90	..	—	—	—	0	—	—	+
41	..	12	8	10	11	23	27	15
								13

+ = Improved

— = Not improved

O = No work or test

been observed. He had become very willing, quiet and well-behaved. He was working well outside the Colony.

No. 51.—At the end of the first six months, no violent outbursts had occurred. He was brighter and more alert. He had become more friendly and worked in the lodge without being prompted. By the end of the first year, he was brighter, even more active and mixed still more freely with the others.

No. 66.—At the end of the first six months, he was better able to understand instructions. He had become eager to learn to read and write. He was more alert, more active and showed a slight improvement in his work. At the end of the year he had improved considerably at his work in the Stores. He was now willing, eager to help and cheerful.

Most of the changes were in the direction of an increase in mental activity but, in some instances, this increase was too great and uncontrolled as the following cases illustrate :—

No. 27.—No change was noticed at the end of the first six months, but by the end of the year, he had become extremely troublesome and spiteful.

No. 29.—During the first six months the condition showed no change but in the second half of the year, he became noisy and troublesome. He now scratched himself when in a temper and his grimacing, present before treatment, became more marked.

No. 32.—Although no change occurred during the first six months in the lodge, he deteriorated at school. During the second six months, he remained stationary in both lodge and school.

No. 40.—In the first six months, he became noisy and a nuisance to others, but showed no alteration at his work. The trouble-making persisted to the end of the year.

No. 42.—No change was noticed in his work in the boot-shop, but he became vicious and aggressive in the lodge during the first six months. Although he was brighter and more active during the second six months, the viciousness and aggressiveness also increased.

No. 44.—He became progressively less responsive during the first and second six months.

No. 45.—By the end of the first half-year, he was more easily upset and a nuisance to others in the lodge, although no change was seen in his work. The alteration in his behaviour in the lodge persisted to the end of the year.

No. 49.—Deterioration at work and in the lodge had occurred by the end of the first six months. This deterioration continued to the end of the year. He became temperamental and stubborn in his work as a tailor's machinist. After 10–11 months of aneurin, aggressiveness developed and he attacked a patient when refused a needle and cotton. He commenced stealing from other patients during the night. When restrained, when in a temper, he burst into floods of tears.

No. 89.—No change occurred during the first half-year, but at the end of the second six-months, she had deteriorated, continually quarrelling and using obscene language.

Although the changes recorded above were for the worse, the extent was insufficient to warrant cessation of the aneurin before the end of the year. In the cases that follow, the over-activity was such that the administration of the preparation was stopped before the end of the year.

(a) At the end of the first six months, this girl had become unbalanced, noisy and was tearing her clothes constantly. This behaviour continued until 3 months after the cessation of the aneurin when she began to behave well, although before the end of the year, she had returned to an unbalanced, noisy state.

(b) He became more noisy and aggressive within a short time of the commencement of the aneurin, which was stopped after 6 weeks. About 3 weeks later a gradual decrease of the noisiness and aggressiveness was apparent. Nine months later, the noisiness and bad temper were occasional and then only when he was annoyed by another patient.

(c) Although no deterioration was noticed in his work, he became more hot-tempered within a week or two of the commencement of the aneurin, which was stopped after 6 weeks. Two to three weeks later a gradual improvement began. During the following 9 months no aggressive acts occurred and the bouts of temper decreased in frequency. In this instance, the number of staff had been increased in the lodge, with a consequent increase of supervision, which may have been partly the cause of the decrease in the number of bouts of temper.

(d) He became more destructive, but began to improve about 1 month after the cessation of the aneurin, stopped 6 weeks after its commencement. Some 6 months later, he showed a marked improvement, becoming less noisy and less destructive.

(e) His temper had become worse before the aneurin was stopped, 8 months after its commencement. Two months later, he was less excitable, more rational in his conversation and took a greater interest in social functions.

(f) Within 3 months of the beginning of treatment he became extremely noisy and dangerous to staff and patients. The aneurin was then stopped. Five months later, he was less often noisy and he was less difficult in his general behaviour than before he began the treatment.

(g) For some months previous to the commencement of the aneurin he had become progressively slower and more apathetic. This process continued during the administration of the preparation and, on account of this change, he was removed from work in the general stores in which he had worked for eight years. He began to strike out at others. The aneurin was stopped and he became more tractable and more easily managed again.

These cases show that some patients improved in their behaviour, some became worse, and some showed no change. Of those that became worse, the adverse change ceased after the aneurin had been stopped for periods varying from two weeks to three months, suggesting that vitamin B₁ is stored in the body for some weeks.

As some cases improved, some remained stationary and others became too over-active on similar diets and doses of aneurin, the conclusion seems justified that each patient requires his own particular dosage which must be adjusted, if possible, a few weeks before an alteration becomes imperative, so that no case is likely to become too difficult.

The social ages showed definite improvement as seen in Table II. Improvement occurred in 15 cases, but in one of these the final S.A. was lower than one before treatment was begun. A decrease had taken place, but this became an increase during the administration of the aneurin. The increases are small, varying from .12 years to two years, but, when it is recalled that the S.A.'s had remained stationary or had decreased before the administration of the aneurin, an increase of any size is remarkable. The S.A.'s increased at various levels from .94 years to 10.8 years. The progressive improvement is not likely to be due to the nursing staff taking a greater interest in those receiving the treatment as only 15 of 41 (36.6 per cent.) showed this type of change.

Improvement in social age is not necessarily paralleled by reports of improvement in lodge or work. Of the 15 cases, 12 showed no corresponding reports of improvement in lodge or work; one improved in work only at the end of both the six-monthly periods; one improved in the lodge only and one had improved in both at the end of each period. The Social Maturity Test is a very fine and delicate instrument for recording behaviour and, no doubt, advances in behaviour would be recorded by this test which would be unnoticed in

TABLE II.—Social ages (in years) of cases who showed increases at ends of both 1st and 2nd six-monthly periods of treatment. Years and months (in numerals) above social ages.

Patient's No.	1946					1947					1948					1949					
	No.	9	11	12	3	6	7	8	9	11	1	3	4	5	6	7	8	9	10	12	1
29	..						.9			.94			1.2						.9	12	1
27	..				1.3				1.3				1.6						1.6	10	1.3
25	..				1.5					1.3				1.8					1.8	10	1.6
56	..			1.77		1.77					1.77					1.83				10	2.1
42	..						1.9				1.9					2.8				12	1.89
68	..				2.9					2.9					3.4				3.4	10	3.2
36	..									3.0			3.2						3.2	10	4.7
41	..										3.5					4.3				12	3.7
40	..										4.0					4.8				12	5.0
46	..										4.2					4.4				12	5.6
74	..																			12	4.8
51	..															5.2				12	5.4
49	..															3.8				12	4.2
62	..																			12	8.8
50	..																			12	9.0
	..																			12	11.7

Period of treatment.

individuals in a lodge containing 60 or 65 defectives or even at their work. In five cases, Nos. 27, 29, 40, 42, and 49, the S.A. improved but the defective became more excitable or aggressive so that no improvement in general behaviour could be recorded. Nos. 27 and 29 had not become more difficult by the end of the first six months although their S.A.'s had already increased.

Although improvements in the intelligence quotients were recorded, both after six- and 12-months' treatment, the improvements were slight and did not affect appreciably the distribution of the patients according to I.Q.

The number of cases at each intelligence quotient is given in Table III, which shows that the number in the lower I.Q. range, below 50, remained approximately constant, no appreciable number increasing in the quotients. In only six cases did an increase of I.Q. take place at the end of both the first and the second six months.

TABLE III.—*Distribution of cases according to I.Q.*

I.Q.	A	B	C	D	E
0—	30	32	7	7	7
1—	2	4	0	0	0
20—	7	10	3	6	4
30—	13	9	6	3	7
40—	14	12	9	8	5
50—	9	8	7	6	8
60—	5	7	4	7	4
70—	2	2	1	1	4
80—	4	2	3	1	0
90—	1	0	0	0	1
100—	0	1	0	1	0
Totals	87	87	40	40	40

A—Previous to treatment (whole series).

B—After six months' treatment (whole series).

C—Previous to treatment (part series).

D—After six months' treatment (part series).

E—After 12 months' treatment (part series).

SUMMARY.

Experiments of giving 3 mgms. daily of aneurin, in addition to that in the normal diet, to 41 defectives for a year, produced a mental change of some kind in 24 cases. An improvement in behaviour or work occurred in nine cases (21·5 per cent.), the improvement being recorded at the end of the first six months and at the end of the second six months of treatment. A rise in the social age, also recorded at the ends of both the first and the second months in each case, took place in 15 (36·6 per cent.) cases. A number, 16 cases, deteriorated mentally during treatment, but 4 of these showed no change

during the first six months. In seven of these 16 the deterioration was sufficiently severe for the aneurin to be prematurely stopped. In each case, improvement, with cessation of the increased excitement, was observed at periods varying from two weeks to three months after stopping the treatment. In all, except two cases, the deterioration consisted of an increase of activity with uncontrolled behaviour. In the two cases, the patients became more apathetic and disinterested.

A dose of 3 mgms. appears to be too great for some cases, each patient requiring an individual amount producing improvement without over-activity.

My thanks are due to my wife and son who assisted with the records and tabulation. To Dr. J. Lyons, Medical Superintendent of Hortham Colony, I am indebted for permission to conduct the treatment and for his interest in the experiment.

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IMPROVEMENT IN MENTAL DEFECTIVES IN COLONIES.

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[Received 12 September, 1949.]

ALTHOUGH one of the important objects of a mental deficiency colony is the return of patients to the general population, the number of cases on licence, or discharged from the provisions of the Mental Deficiency Acts, is not an accurate indication of the improvement-rate. Cases proceed on licence because their behaviour is sufficiently satisfactory for the houses to which they go. A defective may show no change whilst in the colony, but the environment to which he goes may be better than that which he left before entering the colony. Alternatively, the defective may return to the same home circumstances which he left, but he may have improved. All gradations of combinations of change of environment or of defectives occur.

In view of the licence figures failing to indicate the proportion of defectives who improve in a colony, an attempt has been made to estimate the improvement-rate.

METHODS.

Two methods were used. In the first, an investigation was made of medical notes on 540 defectives of all ages, all types and both sexes. The patients had been resident in Hortham Colony for at least one year. Of these cases, 447 (82.8 per cent.) showed improvement in the lodge, in behaviour at school or work, or in social age.

In the second method, a study was made of four aspects of conduct of adult males in a colony. Deterioration was compared with the causes of failure of adult male defectives on licence.

Conduct was divided into :—

- (1) General behaviour.
- (2) Personal habits.
- (3) Work.
- (4) Recreation.

The observation on General Behaviour was an overall, halo effect and included such aspects as irritability, aggressiveness and rudeness. Personal Habits related to cleanliness, tidiness, manners at meals, etc. Work included occupation, either in the blocks as domestic workers, or elsewhere, whether on the farm, engineer's shops, handicrafts, etc. The term Recreation included all types, both in-door and out-door, solitary or social, quiet or noisy. Reading, concentration on the wireless programmes, keeping of pets, walks, etc., were

included. Records were made at the ends of two periods, each of six months duration. The grouping was into Improving, Stationary and Deteriorating for each of the four aspects of conduct. During the first period 121, and during the second period 235, adult male defectives of all grades were investigated. Table I gives the results obtained, with the same staff, for the two adjacent six-monthly periods.

TABLE I.—*Changes in conduct (per cent.) in adjacent six-monthly periods.*

	Period 1				Period 2			
	B	W	H	R	B	W	H	R
Improved	48·7	43·0	22·3	12·4	66·0	53·2	41·2	19·2
Stationary	34·7	47·0	66·9	86·8	27·2	44·7	54·2	78·9
Deteriorated ..	16·5	9·9	10·7	·83	6·8	2·1	6·4	2·1

B = behaviour W = work H = habits R = recreation

The table confirms the general experience that an all-round improvement does not invariably take place in a defective. The figures demonstrate that, in both periods, higher percentages of cases improved in behaviour and in work than in general habits and in recreation. More cases were stationary, in each period, in recreation and habits than in work and in behaviour, but more deteriorated in behaviour and in habits than in work and recreation.

Many defectives changed in the same direction, or remained stationary, in two or three of the aspects of conduct considered here. Comparisons of the proportions of those who deteriorated in all of two or three aspects cannot be made reliably as the numbers are small, varying from seven to one in each combination of aspects. Of those who improved in two aspects, a higher proportion improved in behaviour and work in both periods than in any other two aspects. Of those who remained stationary in two aspects, the highest percentage was, in both periods, in the aspects of habit and recreation. Table II gives the figures, percentages below 10 being omitted as the numbers of cases are few. The defectives who improved in two aspects numbered 28 in period 1, and 54 in period 2, whilst those who showed no change numbered 24 in period 1 and 64 in period 2.

TABLE II.—*Percentage of cases improving or stationary in two aspects.*

	Improved				Stationary			
	B+W	B+H	H+W	W+R	B+R	B+H	H+R	W+R
Period 1	50·0	17·8	3·6	25·0	12·5	29·2	41·6	16·8
Period 2	47·5	35·3	18·5	1·8	15·6	4·7	39·1	32·8

Of the defectives who either improved or remained stationary in three aspects (Table III) 81·8 per cent. of 11 in Period 1, and 72·4 per cent. of 47

TABLE III.—*Percentage of cases improving or stationary in three aspects.*

	Improved			Stationary		
	B+H+W	B+H+R	B+W+R	H+W+R	B+H+R	B+W+R
Period 1 ..	81·8	0	9·2	51·6	25·0	21·9
Period 2 ..	72·4	14·8	10·6	48·9	32·2	11·1

cases in Period 2, improved in behaviour, habits and work. Of 90 who remained stationary in three aspects, 51·6 per cent. of 64 did so in habits, work and recreation in Period 1 and 48·9 per cent. of 29 cases in Period 2.

The total proportion of defectives who changed in a similar manner or remained stationary in any three aspects was 63·5 per cent. in Period 1, and 58·8 in Period 2 (Table IV). The numbers who behaved similarly in all four aspects were small, one case in Period 1 and six cases in Period 2.

TABLE IV.—*Percentages of cases behaving similarly in any three aspects of conduct.*

		Cases	Improving	Stationary	Deteriorating	Total
Period 1	..	121	9·1	52·8	·16	63·5
Period 2	..	235	20·0	38·3	·43	58·8

Similarity occurred in both periods with regard to the relationship between the changes in the four aspects. Of those who improved, the greatest percentage of improvement took place in behaviour, the next greatest in work, the third in habits and the lowest in recreation. Of those who remained stationary, the highest percentage occurred in recreation, the second highest in habits, the third in work, and the lowest in behaviour. This order was, as would be anticipated, the reverse of the proportions amongst those who improved. Of the cases who deteriorated, the highest percentage occurred in behaviour, the second highest in habits, the third in work, and the fourth in Period 1, equal to the third in Period 2, in recreation.

An investigation was made, in a similar manner, of the failures of male defectives on licence. Of 100 consecutive cases returning to a colony, 88 were due to failure in conduct, although, of course, the failures may have been produced by the environment. The remaining 12 cases were returned on account of illness or expiration of licence. Table V shows the percentages of failure in the different aspects of conduct for those returned from licence compared with those who deteriorated in a colony. The proportion who failed in general behaviour was similar in the two groups, but the proportions who deteriorated in personal habits and at work were greater in the colony. This lower percentage with regard to habits may be due to those with whom the defectives were living having a lower standard than that inside a colony. Hence, a change of habits which would be termed deterioration in a colony, would pass unnoticed in certain households. The higher rewards given for work outside a colony may, possibly, be the cause of the lower percentage of failure at work amongst those on licence.

TABLE V.—*Comparison of percentage failure in conduct of males on licence, with males resident in a colony.*

		No.	Behaviour	Habits	Work	Recreation
Licence	..	88	43·2	11·4	9·1	34·1
Colony	..	87	41·4	32·2	19·5	6·9

The part of Table V dealing with recreation shows that a remarkably higher percentage of failure in recreation occurs amongst those on licence, five times that of those in the colony. This higher figure points to the necessity of adequate supervision or control of defectives on licence during their leisure hours, including the choice of the right kind of individuals with whom they can mix socially.

SUMMARY.

1. Amongst 540 defectives of all ages, all types and both sexes, resident in a colony for at least one year, 82.8 per cent. showed improvement in some aspect of conduct.

2. Amongst adult male defectives, improvement in behaviour and in work occurred more frequently than improvement in habits and recreation. All-round improvement in behaviour, work, habits and recreation was unusual.

3. Comparison of adult males failing on licence with similar cases in a colony, showed that failure in behaviour was equal in the two groups. Failure in habits or work was more common in the cases in a colony, whereas failure at recreation was more common amongst those on licence.

My thanks are due to Dr. J. Lyons, Medical Superintendent of Hortham Colony, for permission to use notes of cases.

SYNTHETIC CANNABIS PREPARATIONS IN PSYCHIATRY: (1) SYNHEXYL.

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AND

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FIFTY years ago in a discussion on the pharmacology of cannabis indica, Dixon (1899) said, "Hemp therefore exerts its effect differently according to the preparation used . . . In fits of depression, mental fatigue, nervous headache, and exhaustion a few inhalations produce an almost immediate effect, the sense of depression, headache, feeling of fatigue disappear and the subject is able to continue his work feeling refreshed and soothed. I am further convinced that its results are marvellous in giving staying power and altering the feelings of muscular fatigue which follow hard physical labour . . . It is to be feared, however, that cannabis indica can never become popular until its active principle has been isolated, that is, the isolation of a compound of fixed strength."

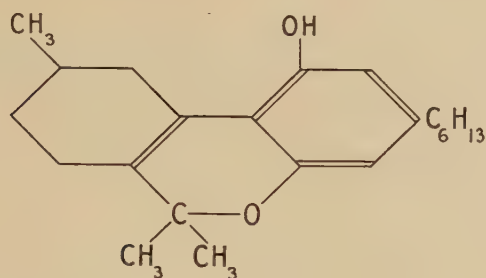
The opportunity to use compounds having fixed strength was accorded to Stockings in 1947 and he reported on clinical trials with Synhexyl. He also laid down criteria for the ideal euphoriant and concluded: "Results of these particular trials would suggest that we have in this class of compounds promising therapeutic agents for the treatment of chronic intractable depressive states."

Later Parker and Wrigley (1947) described the effect of Synhexyl on normal subjects and pointed out its euphorigenic effect. In Stockings' series the trials were made with Synhexyl in a series of 50 patients. These were said to show thalamic dysfunction syndrome and included cases of the depressive-psychotic and the neurotic-depressive types. Numerous case results were quoted to illustrate the points and hope was raised that in Synhexyl, a very promising substance had been found for the treatment of psychiatric conditions.

Recently a quantity of Synhexyl was placed at our disposal for clinical trials and the results and the method of the trial are described below.

Synhexyl is 1-hydroxy-3-n-hexyl-6, 6, 9-trimethyl-7, 8, 9, 10-tetrahydro-6-dibenzopyran, and its structural form is as shown on next page.

There were available the different types of patients usually found in mental hospitals and attending psychiatric clinics and it was decided that it would be profitable to administer the drug to a fairly wide range of patients to see if any particular group could be selected as having been influenced more than another. To this end we treated—



- (1) Psychotics of various types.
- (2) Depressives of various types.

The number originally treated was quite large but we were left, after discharges, etc., with a final figure of 62 patients who had completed the course, of which 16 were out-patients. The dosage employed was at first round about 30 mg. daily but it soon became apparent that doses of this order tended to produce sedation and that more beneficial effects regarding the euphoria would be obtained from smaller doses. This was confirmed also by our personal experience. Consequently in the main a dosage of 10 to 20 mg. daily was employed in this group of patients, though as the trial progressed it appeared that some intractable patients improved generally as the dose was stepped up. This was probably due to its sedative quality. Some of the patients who had previously refused food began to demand it and some of the out-patients said that they felt very much better. Analysis of the results of this study showed that out of the 62 patients treated two groups consistently reported general improvement as judged by their subjective symptoms, by nursing staff observation and by us.

The two groups showing improvement were melancholia and neurotic depressions and it was decided, therefore, to take cases from these two groups, sub-divide them and treat some with active material and some with dummy tablets. The tablets were prepared and designated "Synhexyl A" and "Synhexyl B," and *no one administering the tablets* or assessing the clinical results was aware which contained the active material. The active tablets each contained 5 mg. of Synhexyl and the others contained inert material. The patients were arbitrarily selected from both hospital and out-patient cases and none had previously been treated with Synhexyl. The summarised results of this trial are given below. The degree of improvement being recorded in a standardised way to avoid non-comparable terms:—

SYNHEXYL A.

		Male	Female	Total
Definite improvement	..	3	3	6
Improvement		5	2	7
Slight improvement	..	1	1	2
No improvement		3	8	11
		12	14	26

SYNHEXYL B.

		Male	Female	Total
Definite improvement	..	3	2	5
Improvement		3	6	9
Slight improvement	..	—	2	2
No improvement		7	8	15
		13	18	31

From a study of these results it will be apparent that there is nothing to choose between the therapeutic results in the two series A and B. Some observers have suggested that there is a little extra improvement in the group designated "Synhexyl A," but the batch of tablets designated "Synhexyl B" was the one which contained the active substance, so it can be said that there is nothing arising from this trial that would justify the claim that Synhexyl is a potent substance for the relief of cases of melancholia and endogenous depression. Our findings therefore do not confirm those originally reported by Stockings (*loc. cit.*).

DISCUSSION.

Despite the conclusions reached as outlined above, we know from our own experiences and those of other members of the medical and nursing staff that Synhexyl has definite pharmacological effects and does produce euphoria. This is confirmed also by Adams (1942). Perusal of the literature, Bromberg (1939), Todd (1940), Lancet annotation (1940), Macdonald (1941), Lancet annotation confirms that active fractions of cannabis are euphorogenic. Williams *et al* also (1943), (1946) showed that euphoria was produced in six subjects given *ad lib* doses of Pyrahexyl (U.S.A. terminology) for 26 to 31 days. Personality changes in the direction of lessened inhibitions were observed. E. E. G. studies were also undertaken and it was seen that during prolonged medication the dominant frequencies were markedly slowed. It does appear, however, that despite its obvious pharmacological action Synhexyl is not beneficial to cases usually seen in psychiatric practice. Further evidence on this point is presented by Pond (1948), Watts (1948), and Edwards (1948). It is probable that the failure to influence pathological depression is due to the "wave-like" action of the drug. This may prevent a sustained effect. In normal individuals in whom euphoria was induced this might not be noticed, it not being necessary to "iron-out the trough."

The difference between our results and those of Stockings and the impressions gained from perusal of the literature makes the problem very interesting, and we feel that further work on Synhexyl and allied substances is justified, especially since we feel that a drug of this type might be very useful for tiding over depressions and would help in keeping cases out of mental hospitals. Substances of this type might also be useful in assessing prognosis in psychiatric practice. In large doses it appears to accentuate schizoid symptoms, especially retardation and inaccessibility.

Stockings records the dosage employed as varying from 15 to 90 mgm., the drug being administered in all cases immediately before breakfast. He also reports that the main drawbacks, at present of Synhexyl in the form in which he used it are its insoluble nature and slow and uncertain action and that experiments are at present in progress for producing a water-soluble form with a higher degree of activity. In our series the smaller dose appeared to be well absorbed, this being ensured by the special method of manufacture of the tablets. Therefore, although the dose employed was smaller, we feel that it was an effective one and was based on the observed effect of larger doses, excitation being produced with small amounts and sedation with larger doses.

In no case during this study was there any change in the blood picture, in the urine or blood pressure of any of the patients treated.

SUMMARY.

A trial is described of Synhexyl in cases of melancholia and neurotic depression.

The results do not confirm those reported by Stockings (1947). Synhexyl has marked pharmacological activity and further work on this and similar substances is recommended.

ACKNOWLEDGEMENTS.

We should like to express our thanks to Dr. A. R. Grant, O.B.E., Medical Superintendent, for facilitating this trial, and the medical and nursing staff of Whittingham Hospital for their co-operation. We should also like to thank Roche Products, Ltd., for generous supplies of the material.

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CONGENITAL DOUBLE ATHETOSIS, DEAF-MUTISM AND MENTAL DEFICIENCY : A REPORT OF FIVE CASES.

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CONCURRENCE of the above-named symptoms does not appear to have been reported in the literature. Congenital double athetosis and deaf-mutism usually occur independently of one another. Out of about 1,500 patients at this institution there are 14 with the former condition and 25 with the latter. The relation of the syndrome to its chief constituents may be clarified by a preliminary account of this larger context out of which 3 of the 5 cases here reported are drawn.

Congenital double athetosis has as its central symptom involuntary movements of slow, writhing character, affecting chiefly face, tongue and limbs. There is also the tendency to the adoption of characteristic postures which may lead to permanent deformities. The distal limb muscles are more affected than the proximal. The associated increased tonus of the limbs is at least partly voluntary in origin, brought about to inhibit the movements. There is no pyramidal involvement and the plantar reflexes are flexor.

The degree of disability varies from complete helplessness and speechlessness to a mere maladroitness and clumsiness of the finer and more subtle movements. Of 14 cases here, 2 are unable to walk and practically deprived of speech, 2 have a clumsy and precarious gait and grossly impaired articulation, while the remainder can walk and talk and feed themselves.

Mental deficiency is quite a common concomitant of congenital double athetosis, and is naturally present in most of the cases at this institution. It is seldom severe in degree, nearly all cases being in the dull and backward or feeble-minded class. There appears to be no correlation between the degree of the deficiency and the severity of the athetotic symptoms.

	Uncom- plicated.	With epilepsy.	With deaf- mutism.	Total.
Congenital double athetosis	9	3	3	14
Above with disease of pyramidal system	7	8	—	15

A comparison of patients with congenital double athetosis alone and those also showing signs of pyramidal disease reveals some points of interest :

- (1) The average intelligence of the former group is appreciably higher than that of the latter.
- (2) Epilepsy is rather commoner in the presence of pyramidal disease.

(3) None of the patients with associated deaf-mutism display pyramidal signs.

The table reveals some of these points.

There are 25 cases of deaf-mutism, only one of which has epilepsy, and that particular patient also has athetosis. There is no association with pyramidal disease. The accompanying mental deficiency is mild in most cases, being somewhat similar in degree to that which occurs in uncomplicated athetosis.

It should be noted that neither of the two groups described is homogeneous. For instance, one patient with deaf-mutism also has cretinism, while one case of athetosis is known to be due to Rh incompatibility.

Summarizing the relation of the three patients at this institution with the full syndrome to the two groups described :

- (1) The degree of athetosis is relatively mild.
- (2) Signs of pyramidal involvement are absent.
- (3) The mental deficiency is of mild degree, corresponding to that commonly found in other patients with athetosis or deaf-mutism.
- (4) Epilepsy is present in one case. This is quite common in uncomplicated athetosis, but not significantly so in deaf-mutism.

It may be asked whether the concurrence of athetosis, deaf-mutism and mental deficiency is incidental or whether it is based on a single pathogenesis, and it is convenient to consider this point before describing the cases in detail. On the basis of the facts already given it seems probable that the combination is not incidental. The expected admission rate of patients doubly afflicted would be $14/1,500 \times 25/1,500$. The actual admission rate is $3/1,500$. If the double handicap were to double the likelihood of admission, the actual admission rate would still be 6-7 times the expected rate. Moreover, if the association were incidental, the chance of admitting such a patient who also has pyramidal disease would be slightly greater, and yet there is not one such patient in this institution.

CASE 1.—A. R—, male aged 11 years, 7 months. Examined by Dr. S. Nevin and Prof. Penrose. Estimated mental age 3. I.Q. 26. W.R. doubtful. Cephalic index .82.

History.—Normal birth. Had jaundice three days after birth. Did not walk until 3. Presumably deaf from birth. Mother deaf herself. Patient said to have been mischievous at home and used to play with the fire.

Physical condition.—Diffusely bossed skull; mannerisms and athetosis of hands. Flat-chested. Cardiovascular and respiratory systems normal. Palate and tongue normal. Ears prominent and large. Umbilical weakness. Central nervous system: Reflexes normal. Very poor co-ordination of hands and poor power. Eyes brown. Pupils slightly centrally displaced.

Behaviour.—Attention quite good. Understands signs very clearly. Able to use spoon and fork. Walking good. Slight use of gestures. Clean habits. Not subject to fits.

Family history.—Patient is the fourth of eight children. The other children are all normal. Mother normal except for deafness, which followed scarlet fever at the age of 7 years. No miscarriages. Mother's parents and eight siblings are normal. Siblings' children normal. Father normal. Eldest of family of ten, all of whom were healthy. Father's parents were normal.

CASE 2.—A. L. P—, male, aged 23. Estimated mental age, 11. I.Q. 79. W.R. negative. Cephalic index .77. Height 5 ft. 5 in. Hair fair. Eyes brown. Blood group O.R₂r.

History.—Age of mother at birth 26 years. Mother in good health during pregnancy. Labour difficult. Forceps delivery. Patient nearly died at birth and nearly died again on the third day. There was difficulty in getting the infant to suckle. Fed by spoon and later by bottle. No history of jaundice. Learnt to walk after the age of 2 years. Believed to have had three slight fits in infancy. Noticed to be deaf at an early age.

Physical condition.—Of good physique. Cardiovascular and respiratory systems normal. Tongue and palate normal. Good teeth. Nothing of note outside the nervous system. Central nervous system: Tendon reflexes brisk. Plantar reflexes: Right, flexor; left, indefinite. Pupils react to light. Athetotic movements of tongue, face and neck. Hands: poor co-ordination and tendency to adopt athetotic postures. Gait good.

Behaviour.—Deaf and dumb. Understands gestures. Washes and dresses himself. Feeds with spoon and fork. Collects the laundry and works in the ward. Cheerful, sociable and well behaved.

Family history.—Father dead. Suffered from diabetes. Backward in learning to walk and talk. Was, however, a shipowner's cashier and in a good financial position. Father's mother alive and well. Normal. Mother alive and well. Of normal or superior intelligence. Was a hospital nurse. Her siblings are normal. She knows of no physical or mental disorders in her family or that of her late husband. No consanguinity. Patient is the eldest of two siblings. The other is a girl of 20 years who is normal.

CASE 3.—R. W. T—, male, aged 30 years 5 months. Estimated mental age 10. I.Q. 67. W.R. negative. Cephalic index .79. Height, 5 ft. 2 in. Hair dark. Eyes brown. Blood group O. R₁r.

History.—Age of mother at birth 30 years. No precise information regarding birth available, but had jaundice at birth, which lasted for several weeks. Was able to walk and talk at 6 years, but how long before that is not certain. Has had measles and chicken pox. At age of 10 years was said to have been spiteful and mischievous.

Physical condition.—Of good physique. Cardiovascular systems normal. Palate and tongue normal. Abdomen normal. Stiffness of right leg due to tuberculosis of the right knee-joint. Central nervous system: Tendon reflexes brisk and equal; plantar reflexes flexor. Athetotic movements of tongue, neck face and hands. Gait clumsy but quite good. Some increased tonus of limb muscles.

Behaviour.—Deaf and dumb. Pays attention and understands signs well. On one occasion drew a rough but recognizable outline of his leg with an arrow pointing to the place where the plaster was hurting him. Was able to wash before the joint disease developed. Feeds with spoon and fork. Used to do simple work in the ward. Cheerful and sociable.

Family history.—Whereabouts of parents now unknown. The father was an electrician of normal mentality. His parents were normal. The mother was normal and her parents were normal. The patient is the youngest of three children. The eldest was alive and well at the age of 12 years. The second died of whooping-cough at the age of 5 weeks.

CASE 4.—P. A. C—, female, aged 17. Mental age 12. I.Q. 80 (Drever-Collins). W.R. negative. Cephalic index .786. Blood group, O. R₁r. Hair dark. Eyes hazel.

History.—Illegitimate. Early history unknown.

Physical condition.—Good physique and attractive appearance. Palate and tongue normal. Cardiovascular and respiratory systems normal. Abdomen normal. Nervous system: Pupils react to light and accommodation. Tendon reflexes normal. Plantar reflexes flexor. Muscular hypotonia. Involuntary movements of limbs and of face, neck and shoulders. These are slighter than in the other cases and rather more choreiform than athetoid.

Behaviour.—Deaf and dumb. Washes and dresses herself. Walks well and feeds without any difficulty. She is now beginning to write and has learnt to say some words spontaneously as a result of lip-reading, although she has not had any special training. She is usually sociable and pleasant but is spiteful at times.

CASE 5.—An abstract of this case was kindly supplied by Dr. Kirman, of the Fountain Hospital.

J. L. F—, male, aged 5 years 4 months. On admission (aged 3 years 6 months): Height 38 in., weight 30 lb. Cephalic index .77. Left-handed.

History.—Patient is the result of the second pregnancy. The first child was a stillborn but apparently normal baby. There was a post-partum haemorrhage and the mother was transfused. Patient born in 1944 and suffered from icterus gravis. His blood was noted to be Rhesus positive. During the third pregnancy the mother was noted to be Rhesus negative and to have a rising titre of anti-D. substance in her serum. The father was Rhesus positive (homozygous).

Progress of patient.—(May, 1949). Found to be deaf-mute and also to exhibit a number of choreiform movements. Very restless. Unable to wash or dress himself. Totters a good deal but gait improving. Willingly obeys, but not spoken commands. A mental test in November, 1948, gave him an I.Q. of approximately 49 on the Merrill Palmer.

DISCUSSION.

There are various causes of athetosis, as also of deaf-mutism, acting upon the organism at different stages of development. At what points do the two paths of possible pathogenesis coincide?

Hereditary causes.—According to Denny Brown, "the affection (congenital athetosis) sometimes is hereditary, more often familial, but usually isolated." The hereditary tendency in deaf-mutism is more commonly in evidence, the mode of inheritance being usually recessive, autosomal or sex-linked. There is, however, no known genetic connection between the two diseases.

No familial or hereditary tendency could be established in the cases reported.

Prenatal causes.—Of these the most interesting possibility is Rhesus incompatibility between mother and foetus. The occurrence of athetosis associated with kernicterus of this origin is well known. We know of no published evidence favouring Rhesus incompatibility as a cause of deaf-mutism. The evidence for case 5 being produced in this way is, however, rather strong, since the child is known to have had icterus gravis. The history of Case 3 is, perhaps, similarly suggestive, but not convincing. The affected patient was the third of three children and had jaundice at birth which lasted for three weeks. In no case here reported can the possibility of this origin of the disease be ruled out, for all the patients are heterozygous positive, but on the basis of the history Case 2 is the least likely to be so caused.

Birth injury.—Norman reported three cases of mental deficiency associated with pyramidal involvement. Athetosis was present in one of these cases and the pathological findings showed *état marbré* associated with other changes characteristically due to birth injury, of which there was also a strong family history. Evans found a significant association between congenital athetosis on the one hand and primogeniture, prematurity and a history of birth injury on the other. There therefore appears to be evidence that birth injury may sometimes produce congenital athetosis.

Evidence of any causal connection between birth injury and deaf-mutism is more scarce, but Hallpike reported a case of deaf-mutism in which an unhealed fracture of the labyrinth capsule on the right side was found, probably due to birth injury.

The history of Case 2 is strongly suggestive of birth injury.

No definite conclusions as to aetiology can be drawn. It appears to us, however, that the causes most favoured by the evidence available are Rhesus factor incompatibility and birth injury. The combination of symptoms may, of course, be sometimes due to one factor, sometimes another, and sometimes to an incidental association of unrelated events. For instance, the author has seen a patient with athetosis and deaf-mutism in whom the former condition is due to kernicterus, the latter to bilateral mastoidectomy performed at an early age. (I am grateful to Dr. V. Cowie for drawing my attention to this case.)

The occurrence of deaf-mutism and athetosis as a result of birth injury has some pathological evidence to support it. This paper provides some clinical evidence that Rhesus factor incompatibility may also give rise to the syndrome. We know of no pathological findings that would account for deaf-mutism of this origin.

SUMMARY.

(1) Five cases of a syndrome characterized by mental deficiency, congenital double athetosis and deaf-mutism are described.

(2) A brief account is also given of the athetotic and deaf-mute "population" from which three of the five cases are drawn.

(3) The aetiology is discussed.

I am grateful to Prof. Penrose for the case notes of Case 1 and to Dr. Kirman for the abstract of Case 5; also to Dr. Hilliard for permission to make use of this case and to Dr. Taylar for allowing me to make use of the material at this institution.

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SPONTANEOUS HYPOGLYCAEMIA AND DIABETES MELLITUS ASSOCIATED WITH THE INSULIN COMA THERAPY OF SCHIZOPHRENIA.

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THIS paper is concerned with two schizophrenic patients showing unusual complications of Sakel's insulin coma therapy. The first had a series of attacks of spontaneous hypoglycaemia apparently uninfluenced by the temporary withholding of insulin; the other developed diabetes mellitus a short time after finishing his treatment.

This is the first time that either of these complications has been encountered in a series of over 1,000 cases treated by this method at Crichton Royal. Furthermore, neither reference to the literature nor enquiry at other centres with considerable experience of the treatment has revealed any account of similar occurrences in relation to Sakel's insulin coma therapy.

It is hoped that the cases may be of interest not only because of their rarity, but also in relation to the general problem of carbohydrate metabolism and the action of insulin thereon.

CASE 1.—A. K—, aged 23, a house painter by occupation, was admitted to Crichton Royal on 6.iv.48 and diagnosed as a case of paranoid schizophrenia. His main symptoms were delusions of persecution, ideas of reference and occasional auditory hallucinations. He had had a previous attack in 1945 while serving in the Navy. On that occasion he made a good recovery after a course of insulin coma therapy, which passed without incident and he was discharged from the Navy in February, 1946.

During the present illness he showed some insight and voluntarily sought treatment. His personality was well preserved and it was considered that the prognosis for this attack was good and that he would benefit from another course of insulin coma therapy.

Physically he was a well nourished man of athletic habitus, and routine examination did not reveal any abnormality. He commenced treatment on 26.iv.48, and had his first coma with a dose of 200 u. of insulin on 4.v.48. His progress after this was as follows:

- 5.v.48: Coma on 200 u.
- 6.v.48: Urticarial rash on abdomen. Only sopor on 200 u.
- 7.v.48: Rash more widespread. No reaction to 230 u. Benadryl mgm. 100 *t.d.s.* started.
- 8.v.48: Urticaria improved. No reaction to 250 u. of a different brand of insulin.
- 9.v.48: Sunday. No treatment. Urticaria greatly improved.
- 10.v.48: Urticaria cleared. No reaction in the forenoon to 250 u., but at 10.30 p.m. went into sopor. Recovered after 140 ml. of 33 per cent. (w/v) sucrose solution.
- 11.v.48: Drowsy after 260 u. No sopor or coma and was able to drink 33 per cent. (w/v) sucrose solution.

12.v.48: Went into coma at 1 a.m. Recovered after 570 ml. of 33 per cent. (w/v) sucrose solution by nasal tube. No insulin. Benadryl discontinued.

13.v.48: Forenoon, 30 min. coma after 270 u. After waking he was confused and wept for a while. Later he vomited and was given 100 ml. of 33½ per cent. (w/v) glucose solution i.v. Rather tired all afternoon, but otherwise normal.

14.v.48: At 2.10 a.m. went into coma and required nasal feed. Despite this he received 200 u. at the usual time and had a 30 min. coma.

15.v.48: Perspiring profusely at 1.30 a.m. and given 280 ml. 33 per cent. (w/v) sucrose solution. In sopor at 7 a.m. and had to be fed nasally. No insulin.

16.v.48: Signs of hypoglycaemia at 6.30 a.m. Recovered quickly after drinking 850 ml. 33 per cent. (w/v) sucrose solution. No insulin.

17.v.48: Received 180 u. at 7.30 a.m. and went into coma at 8.30 a.m., i.e. about 1½ hours earlier than usual.

18.v.48: 180 u. at 7.30 a.m. In coma at 9.20 a.m. Roused normally. At 10 p.m. he showed signs of hypoglycaemia, which cleared after 280 ml. 33 per cent. sucrose solution. It was decided to discontinue the insulin therapy.

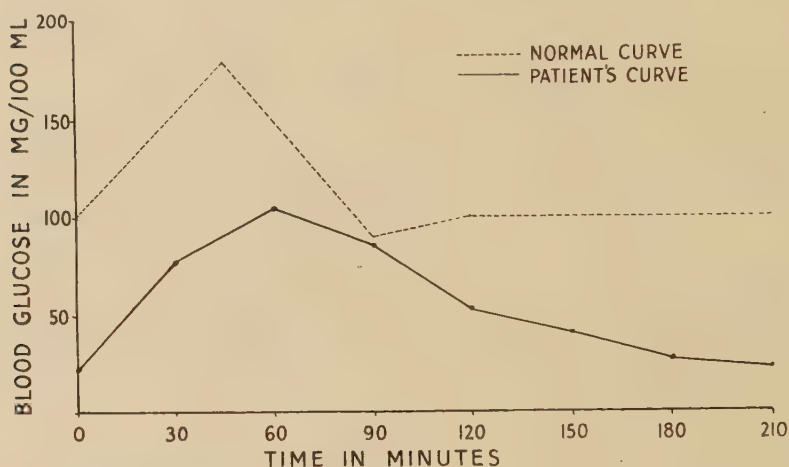


FIG. 1.

19.v.48: In sopor at 5.45 a.m. and recovered after 280 ml. 33 per cent. (w/v) sucrose solution. Although he received no insulin he went into sopor at 8.10 a.m. and was given 100 ml. of 33½ per cent. (w/v) glucose solution i.v.

20.v.48: Showed hypoglycaemic symptoms in the morning and at 8.10 a.m. his blood glucose was 21 mgm./100 ml.

21.v.48: Showed gross signs of hypoglycaemia when sent for a glucose tolerance test at about 9 a.m. The fasting blood-sugar level was 16 mgm./100 ml.

22.v.48: Signs of hypoglycaemia in the morning. An extra meal at 10 p.m. was instituted.

23.v.48: No signs of hypoglycaemia.

24.v.48: Glucose tolerance test repeated. Fasting level was 21 mgm./100 ml., but he did not have any clear symptoms of hypoglycaemia (Fig. 1).

During the ensuing couple of weeks various tests were carried out. Insulin sensitivity was found to be normal. In tests of liver function the serum colloidal gold reaction was negative and although the Galactose Index was 195, which is above the generally quoted limit of normality, it was not considered to be significant when considered together with other factors. Urinary diastase was normal and the excretion of 17-ketosteroids was 16.8 mgm. in 24 hours. X-ray of skull was normal.

On three occasions blood was taken for glucose estimations at two-hourly intervals during the day and night. Readings at midnight and 2 a.m. were low on each occasion.

On 7.vi.48 the extra evening meal was dispensed with, as the patient had not shown hypoglycaemic symptoms for some days. Two-hourly estimations on 10-11.vi.48 gave the following blood-glucose readings; no signs of hypoglycaemia were present at any time.

4 p.m.— 86 mgm./100 ml.	4 a.m.— 42 mgm./100 ml.
6 p.m.— 58 "	6 a.m.— 58 "
8 p.m.—107 "	8 a.m.— 49 "
10 p.m.— 63 "	10 a.m.—167 "
Midnight— 26 "	Noon—121 "
2 a.m.— 23 "	2 p.m.—104 "

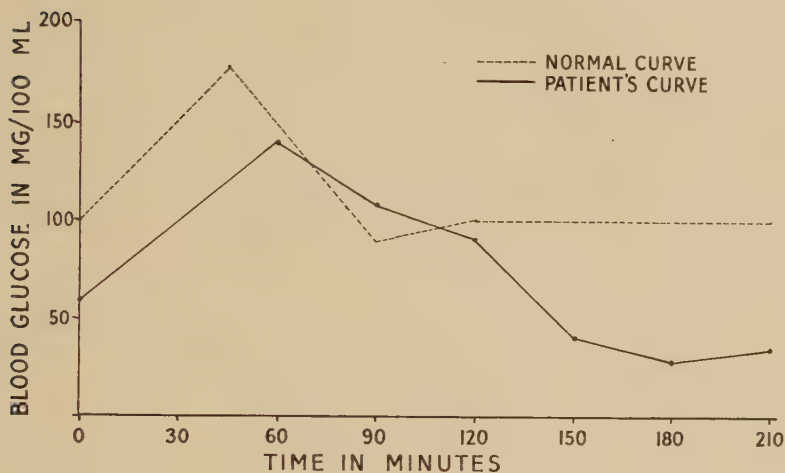


FIG. 2.

Meals were taken at 8 a.m., 1 p.m. and 6 p.m.

As a glucose tolerance test on 12.vi.48 gave a curve (Fig. 2) which appeared to be within normal limits although the readings at 3 hours and 3½ hours were low, it was decided to resume treatment cautiously. On 14.vi.48 a trial dose of 5 u. of insulin was given and on the following day 50 u. On each occasion blood-glucose estimations were made at frequent intervals. As the response was normal, it was considered safe to resume the course of insulin coma therapy. This was completed by 31.vii.48 without further incident, the coma dose being 180 u. A glucose tolerance test which was within normal limits was carried out before his discharge on 4.ix.48 in a state of good remission from his attack of schizophrenia.

Summary.

This schizophrenic patient had a successful course of insulin coma therapy in 1945. Three years later he relapsed and was started on another course. During this he had several attacks of spontaneous hypoglycaemia which continued many days after insulin injections had been discontinued. An urticarial rash occurred before these attacks commenced. Blood-glucose estimations showed a gradual return to normal over a period of four weeks and the course was resumed and completed without further incident.

Comment.

Careful history taking failed to elicit any account of previous attacks which might be construed as due to hypoglycaemia. The patient had never taken

particular precautions about his diet and was apparently untroubled either after missing meals or after unduly heavy meals.

At a follow-up interview in May, 1949, he stated that he had not had any hypoglycaemic symptoms since his discharge. He is a good witness and is, of course, very familiar with these symptoms.

The only report of a similar occurrence discovered in the literature is that by Kautzky (1948). His patient was an involutional melancholic of 68 years who had received three courses of modified insulin therapy within a year. The dose had been as high as 110 u., and he had gone into coma on five occasions. A fortnight after the last treatment with insulin he started hypoglycaemic attacks, with blood-sugar levels as low as 20 mgm./100 ml., nightly between 12.30 a.m. and 6 a.m. After a fortnight an extra meal at midnight was introduced and this stopped the attacks. After a further ten days this meal was omitted, but the attacks did not recur up to the time of his death from bronchopneumonia 8 months later. At autopsy changes in the pancreas due either to arteriosclerosis or chronic pancreatitis were found, but were not considered causative.

In trying to find an explanation of the transient spontaneous hypoglycaemic attacks one must bear in mind Conn's (1940) assertion that on a normal diet depression of the fasting blood sugar below 50 mgm./100 ml. indicates an organic cause for the hypoglycaemia with but few exceptions.

Hypofunction of the pituitary and of the adrenal cortex are alleged to be occasionally responsible for spontaneous hypoglycaemia, but neither clinical nor laboratory findings suggested a deficiency in our case. The Galactose Index was rather high, but it was not considered significant, as the other test of liver function were normal and the glucose tolerance curve was not of the high plateau type observed in cases of hepatic insufficiency.

The type of glucose tolerance response called by MacLean (1926) the "lag" curve and by Lawrence (1936) oxyhyperglycaemia, is believed by Hastings-James (1949) to account for most cases of idiopathic spontaneous hypoglycaemia. It did not occur in our case. It is also relevant to note that the patient had not undergone any gastric "short-circuiting" operation; hypoglycaemic symptoms have been noted to occur in patients after this type of operation when the rapid emptying of the stomach produces rapid absorption of glucose and a "lag curve" effect.

A short period of unusual stimulation of the islet cells is the most probable explanation of the recorded series of events.

It is unlikely that the allergic reaction was in any way relevant; similar reactions take place in a proportion of all patients receiving insulin without usually affecting the dosage. It seems possible that there may be some relationship between our observation and the phenomenon whereby insulin dosage can be greatly reduced or even stopped for a while in certain early cases of diabetes which have been treated energetically. This presumably depends either on a sensitization to insulin or on a temporary stimulation of the islets, but, unfortunately, the exact mechanism is not known.

CASE 2.—S. S—, a Jewish youth, aged 18, a pharmaceutical student, was admitted to Crichton Royal on 8.vii.48. He was of leptosomatic habitus, and

routine physical examination did not reveal any abnormality. Urine analysis on admission gave normal results.

Although no member of the family had been in a mental hospital there was evidence of psychotic traits on father's and mother's side. The paternal grandfather was described as "solitary, slovenly, miserly and liable to try to interfere with his daughters and with other women." The patient's mother had short "nervous breakdowns" after the birth of each of her three children. The father was of pyknic habitus and a first cousin of the father developed diabetes at the age of 15 years and died at the age of 19 of pneumonia.

The parents stated that the patient, the first child, was wanted, but that because of her "nervous breakdown" the mother was unable to breast feed him. He was bad tempered and difficult with his food. He developed normally, passing the various milestones at the usual times. He was mischievous, and when very young he used to wander away from home frequently. His parents were both at business during these years and did not spend a great deal of time with him.

The patient's performance at school was very variable. The teachers complained that he day-dreamed and did not make use of his talents. He matriculated at 15 years. He disliked games and was a poor mixer.

His behaviour has given rise to some concern since about the age of 14 years. He became very irritable and quarrelled constantly with his younger sister and brother. When he was about 16 years he brought home a note-book from school and showed it to his parents. It contained a detailed description of another boy who masturbated in school and of the excitement which this induced in himself. This note-book was also a record of the emotions he had experienced since his first day at secondary school, mainly about his sexual interest in other boys. It recounted how he was attracted, disgusted and excited by watching them masturbate.

During the year prior to admission the patient became more withdrawn and suspicious, complaining that his parents were treating him badly and that people were laughing at him. He became dirty in his habits and hid dirty clothes on top of cupboards. Nevertheless, he was apprenticed as a pharmacist and, as far as is known, worked satisfactorily. It appears that he had some insight, as it was at his own request that he was taken to see a psychiatrist.

On admission he was quiet and co-operative, but was soon observed giggling frequently to himself. He spent much of his time striding up and down the ward "practising keeping my back straight." His stream of talk was free and for the most part coherent, but occasionally there was evidence of thought disorder. He produced many neologisms but did not use them in conversation. He stated that words kept coming into his head because of his boredom. Examples which he gave were "fillible, rigarallo, sutent, tervinate, imbucibly, susquinaceous." Of the latter he said "It means something less than the nature of a quin. I went to a library and got out a book by a man called Quin: it was on spiritualism, probably a coincidence, really."

Objectively he showed shallow and incongruous affect and he made complaints such as "my emotions have disappeared, I feel dried up inside." He had marked ideas of reference. He described a great number of coincidences in a film which he had recently seen and how they all applied to him.

Symptoms of depersonalization and derealization were prominent. He complained, "I don't know what is me and what isn't. When I look in the mirror my face seems different from before," and again, "There is a certain sense of unreality about everything, everything seems very sharp, my senses are very acute. . . . I have no sense of perspective when I look out of my body."

Intellectual functions tested by Raven's Matrices Test and the Mill Hill Vocabulary test were found to be above average (Grade 2 in both tests). The diagnosis schizophrenia was made and he started a course of insulin coma therapy on 19.vii.48. The course passed without incident except for a break of one week, when he had tonsillitis. He had 53 comas with 7 insulin fits. His coma dose varied between 100 u. and 70 u. Treatment finished on 2.x.48.

The patient showed considerable improvement. He lost his ideas of reference and became more sociable. There was no longer any evidence of thought disorder. The symptom of depersonalization, however, remained and in fact he considered that they were more marked than before. Thyroid was given as Elityran Tablets (Bayer) in progressive doses. During the next few weeks there seemed to be a slow but steady improvement in his mental state. He complained of tiredness,

however, and began to lose weight early in November. This was thought to be due to the Elityran, which was discontinued on 11.xi.48. However, loss of weight continued and polyuria and polydipsia developed. Urine tested on 7.xii.48 gave a strongly positive Benedict's reaction and a positive Rothera's test. The following day a glucose tolerance test was performed which gave a typical diabetic curve with a fasting level of 208 mgm./100 ml. and rising to a peak of 417 mgm./100 ml. at 1½ hours (Fig. 3). Treatment with increasing doses of soluble insulin and a reduction of carbohydrate in the diet was commenced and by 31.xii.48 the diabetes was

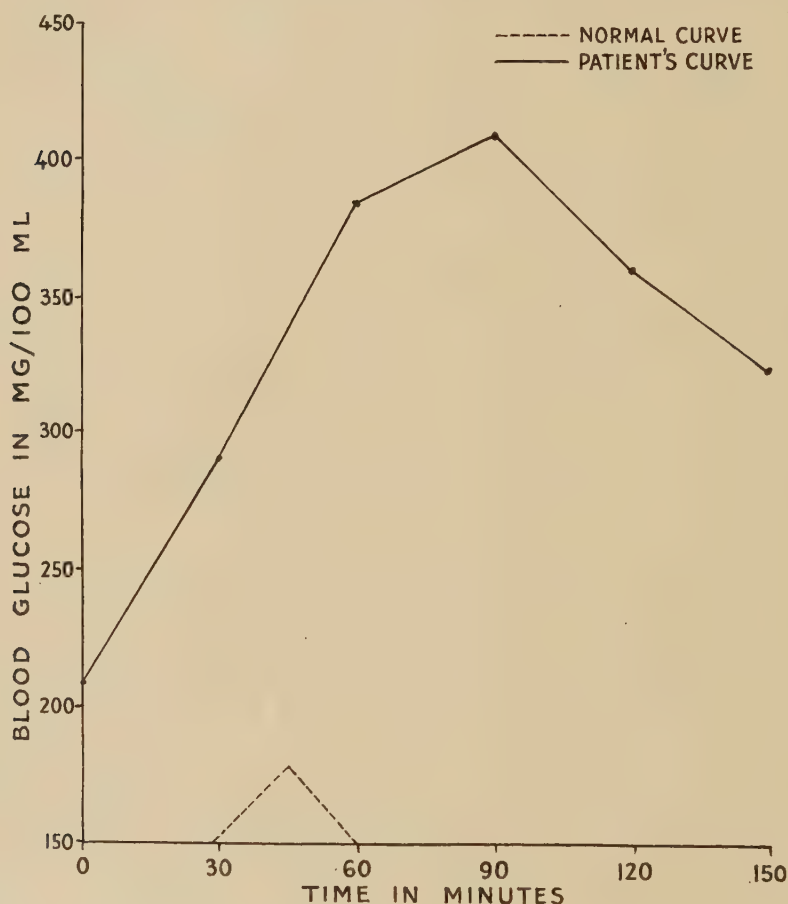


FIG. 3.

controlled with 40 u. morning and 35 u. evening. A change to protamine zinc insulin 50 u. + soluble 20 u. was made on 15.i.49. It was found possible to reduce this dose progressively until by 31.i.49 he was free of symptoms and showed no glycosuria although without insulin. A glucose tolerance curve at this stage did not rise above 190 mgm./100 ml., but showed a delayed return to normal.

The patient was discharged on 15.ii.49, although still experiencing depersonalization phenomena. It was considered reasonable to give him a trial in a different environment, since most of his psychotic features had cleared.

He had to be readmitted on 15.iii.49. His mental state had deteriorated considerably, he was dirty and untidy, giggling incessantly to himself during interviews, although professing to be in a state of great distress. He retained his symptoms of depersonalization and had marked passivity feelings.

His physical condition had also deteriorated. Urine contained glucose 0.4 gm./100 ml. and Rothera's test was "slightly positive." Fasting blood sugar was 104 mgm./100 ml. and the glucose tolerance curve was frankly diabetic.

Summary.

A Jewish youth developed diabetes mellitus after treatment by insulin coma therapy for a typical attack of hebephrenic schizophrenia characterized by thought disorder, ideas of reference, incongruous affect and symptoms of depersonalization. A first cousin of his father had been a diabetic, presumably also of the early insulin-sensitive type.

Comment.

This case has been described at some length in order to establish firmly the diagnosis of schizophrenia, since reports in the literature give the impression that the occurrence of diabetes mellitus in patients suffering from schizophrenia is remarkably rare. It is, of course, possible that this impression is false and that statistically, it could be shown to be due to chance, as diabetes is relatively uncommon in the age groups when schizophrenia is frequent.

Six cases of true diabetes were found among 279 Jewish schizophrenics by Ligterink and Simons (1936). They reported that all their cases belonged to the pyknic type and all showed an hereditary disposition for manic-depressive psychosis. This they considered to be in keeping with Reiter's (1927) suggested explanation of the rare combination of diabetes and schizophrenia, namely, that "Pyknics develop diabetes mellitus because their habitus predisposes to vegetative kinds of metabolic disorders, whereas leptosomes do not develop diabetes."

The patient described in the present paper was not pyknic, neither could an hereditary disposition to manic-depressive psychosis be shown, although the nature of the mother's recurrent psychosis could not be clarified.

Single cases of the concurrence of diabetes and schizophrenia have been reported, as, for example, by Moellenhoef and Moellenhoef (1942). Their case was diagnosed as a diabetic at the age of 15 and as schizophrenic at 26 years. Kasin and Parker (1943) reported one case; in reviewing the literature they concluded that the only other fully substantiated case previously reported was that of Hofman-Bang (1928). They particularly stress the importance of distinguishing psychotic pictures associated with diabetes itself from true schizophrenia occurring with diabetes.

It is difficult to voice an opinion on the relationship between the insulin coma therapy and the onset of diabetes in the present case. No similar incidence could be found on perusing the large literature on complications during this treatment. It seems that the patient had an hereditary predisposition to diabetes. In view of Harris's (1949) comments on the incidence of cousin marriages among the parents of patients developing the early insulin-sensitive type of diabetes, it may be noted that there was no blood relationship between his parents. Looney and Cameron (1937) have shown a decrease of sugar tolerance for a period after a course of insulin coma therapy and suggested that it was due to a stimulation and sensitization of the adrenal mechanism.

On the other hand, Haist *et al.* (1940) showed that diabetes can be prevented in a dog receiving injections of anterior pituitary extract provided that insulin is given at the same time. They even suggested the prophylactic use of insulin experimentally in families with marked heredity but, of course, not in coma doses.

In the absence of an explanation it is tempting to assume an interference with genetically susceptible hormonal mechanisms, but such an assumption can only be speculative.

SUMMARY.

Two unusual complications of the insulin coma therapy of schizophrenia are reported.

The first patient had attacks of spontaneous hypoglycaemia over a period despite the withholding of insulin. Blood glucose studies are recorded. They showed a gradual return to normal over a period of four weeks.

The second patient developed diabetes mellitus within about a month of completing a course of insulin coma therapy. It is suggested that this patient was genetically predisposed to diabetes mellitus.

Comment is made on the rarity of reports in the literature of the occurrence of schizophrenia and diabetes mellitus in the same patient.

ACKNOWLEDGMENTS.

My thanks are due to Dr. P. K. McCowan for permission to report these cases and to Dr. W. Mayer-Gross for his interest and helpful criticisms.

The blood glucose estimations were carried out by Mr. J. W. Walker according to the method of King *et al.* (1937).

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It is much regretted that these illustrations to Dr. R. KLEIN's paper on "**Clinical and Biochemical Investigations in a Manic-Depressive Psychosis,**" January, 1950, p. 293, were omitted.

D. FIRST DAY OF DEPRESSIVE PHASE.

M. " " " MANIC "

N. " " " NORMAL "

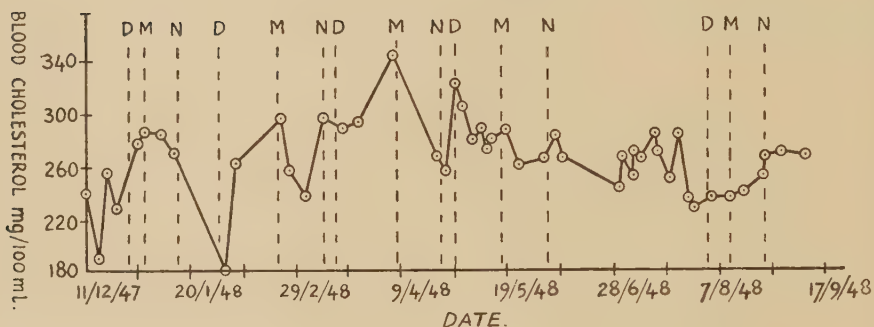


FIG. I. VARIATION OF BLOOD CHOLESTEROL.

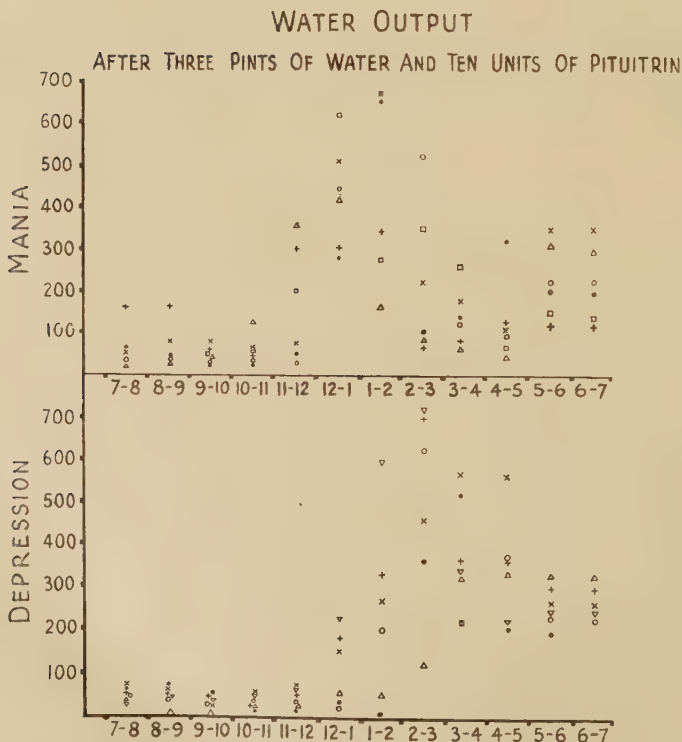


FIG. 2.

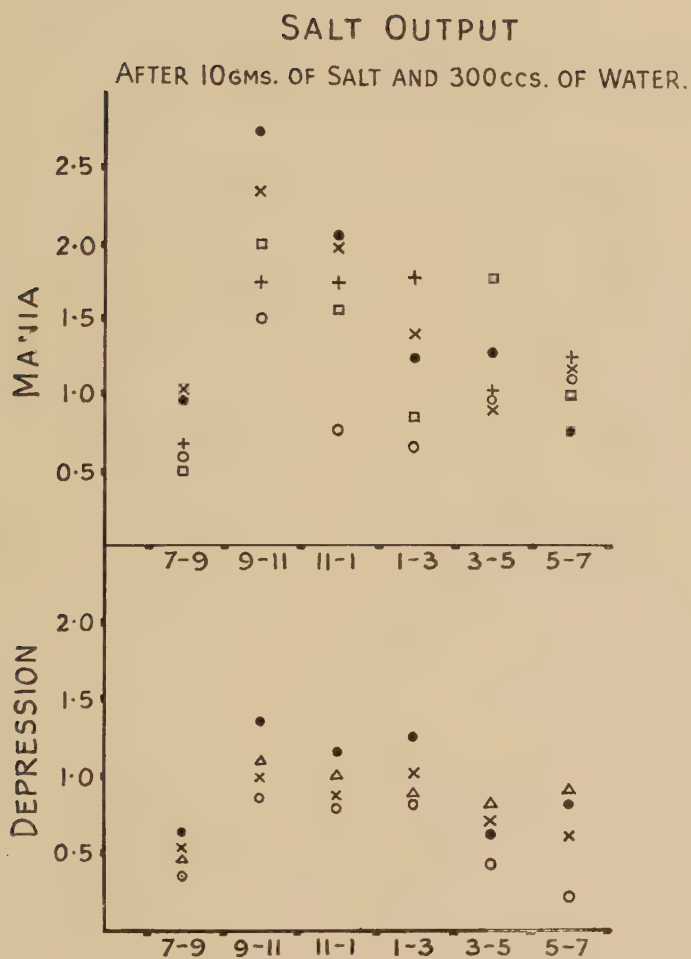


FIG. 3.

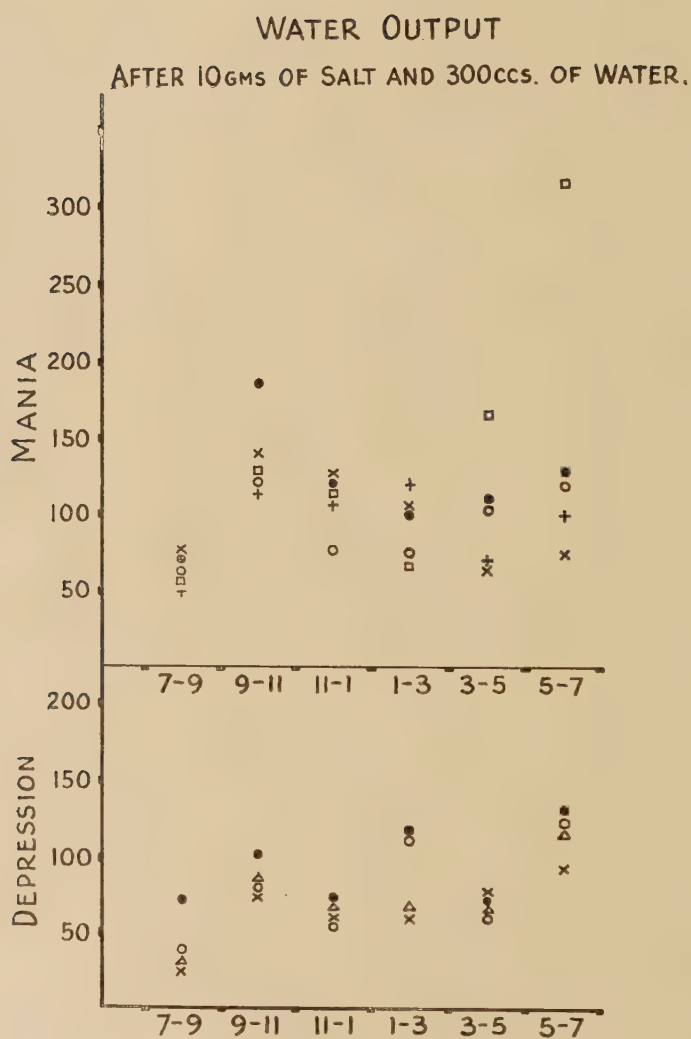


FIG. 4.

CLINICAL AND BIOCHEMICAL INVESTIGATIONS IN A MANIC-DEPRESSIVE WITH SHORT CYCLES.

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(Received 1 October, 1949.)

RESULTS of a previous investigation of manic-depressive psychosis with a continuity of cycles of short duration (Klein and Nunn, 1945) seemed to justify further study of this group. As such cases suitable for investigation are rare, we are again reporting observations on a single case, although the cycles were not as short and regular as in the earlier case. The patient at the time of his last admission to this hospital (in 1944) was aged 40, married, had a healthy child of 16, and was an employee of a tobacco factory. He was said to have been always very quiet and reserved, and had no history of mental illness before joining the Army in 1941. He went to the Middle East in July, 1942, and began to feel listless, tired and sleepless for the first time at the beginning of 1943. After spending four weeks in a military hospital he still felt low on returning to his unit, but soon afterwards was full of life; in his own words, "I could tear anything down." A fresh period of depression set in later, and he was sent to a military mental hospital for six months, during which time he apparently changed several times from a depressive state into a manic one in which he felt "overstowed with vitality," "with the energy of ten men." From this hospital he was returned to England and invalided from the army in October, 1943, at which date he first became a patient in this hospital. An initial depression of about three weeks was followed by a manic condition, and on becoming more settled he took his discharge (at the beginning of December, 1943). In February, 1944, he was readmitted in depression, but went out again whilst in moderate mania in April. Whilst at home he continued his work in the factory, but in September, 1944, was once more admitted to hospital and has since remained. From the latter date till October, 1948, depressive periods have alternated with manic conditions. Wide variations have been noted in the duration of the two phases; at the beginning of the observation period of 21 cycles the manic state lasted longer than the depression, whilst in the last year the reverse was usually true. Manic periods varied between one week and 35 days, with an average of 18 days, while the variation shown by depressive phases was between 6 and 24 days, with an average of 13 days.

Transition from depression into mania was always sudden, and occurred regularly at night. Failure to sleep was invariably the first sign of the change; in the course of the night he became restless, talkative and irritable, and it was difficult to keep him in bed or restrain him. From then on he was from

four to six days at the height of his manic phase. Sleeplessness persisted, he rose early, was boastful and quarrelsome and somewhat difficult to manage, and in between he had spasms of emotional outbursts of self-pity and crying. This phase was followed by a more settled state, when he gradually returned to a normal behaviour pattern, appearing emotionally stable, active and interested; this condition lasted for a fortnight on an average. The next stage in the cycle commenced with tiredness and listlessness in the morning, accompanied by disinclination to get up, and loss of appetite though during the course of the day his spirits improved, and he regained his normal activity. Two to four days later a deep depression set in, when he did not speak at all spontaneously, and little in conversation. He stayed in bed all day when allowed to, eschewed company, and felt incapable of any activity. When out of bed he sat about, solitary and unoccupied; he appeared melancholy, and when asked about his condition complained that he felt tired, sleepy, without energy and interest. Though his night's sleep was prolonged up to ten hours, he was frequently found dozing during the day, and he had to be prompted to take his meals as his appetite was poor. The intensity of the depression varied to some extent. When prolonged it usually became less deep in the later stages. He was brighter and more active in the afternoon, occupying himself with reading, listening to the wireless or participating in games which did not involve physical effort.

The cycles described continued to 1 September, 1948, and on that date a depression set in which has persisted in a moderate form ever since, exhibiting the usual characteristics of the later stages of his former prolonged cyclical depressions. Though less active he was up during the day and did a reasonable amount of physical exercise; he helped in the ward and participated in games. Whilst for 8 months in the depression his weight increased by over 2 stone.

Blood pressure, pulse and temperature were taken daily over a number of cycles. Blood pressure was generally slightly over 120/70 mm. Hg in the manic and about 100/60 mm. Hg in the depressive phase, but these values were not absolutely constant, for higher figures in the depression and lower in the mania could occasionally be observed. The same applied to the pulse rate, which ranged usually between 70 and 84 in mania and 60 and 72 p.m. in depression. There was no definite difference in temperature between the two phases, nor could any difference in the blood picture be established. Body weight tended to rise in depression and fall during mania, the extent varying according to the duration of the phase.

BIOCHEMICAL INVESTIGATIONS.

During the biochemical investigations the patient, as in the case previously reported, was kept on a constant diet with constant fluid and salt intake. He was kept in bed for a number of cycles, as well as on days when special tests were carried out. Urine was collected every 12 hours under toluene or chloroform, and the volume, specific gravity and pH determined. No drugs were given.

The relatively long duration of one particular period of investigation permitted daily determinations through several cycles on only a limited number

of urine and blood constituents, i.e. urinary excretion of creatinine (estimated by the method of Folin), sodium chloride (Volhard's method), calcium (Shohl and Pedley, 1922), inorganic phosphate (uranium acetate method), and ammonia and blood levels of haemoglobin, haematocrit, and non-protein nitrogen. Estimations were also carried out several times in each phase and for several cycles of blood calcium and magnesium (method of Kramer and Tisdall, 1921), potassium (Jacobs and Hoffman, 1931), sodium (Noyons, 1939), chloride (Haslewood and King, 1936), inorganic and ester phosphates (Fiske and Babbarow, 1925), total nitrogen (by micro-Kjeldahl), creatinine (Folin and Wu, 1919) and cholesterol (Sackett, 1925), and of urinary excretion of 17-ketosteroids and cortin. In the urine steroid analysis the methods employed for the isolation, fractionation and estimation were the same as those described in a recent communication from these laboratories (Reiss, Hemphill, Gordon and Cook, 1949).

Of the constituents investigated, abnormal values were shown only by blood cholesterol and by urinary excretion of cortin and β -17-ketosteroids. Cholesterol (Fig. 1) usually varied between 250 and 300 mgm. per 100 c.c., and there was a tendency for peak values to appear during the depressive phase. Abnormally high values for cortin and β -17-ketosteroids excretion were sometimes observed, and detailed results for these estimations will be given in a separate communication (Reiss, Hemphill, Gordon and Cook, 1949).

Daily measurements of total urine outputs and chloride excretion over a number of cycles gave no indication of retention during the depressive phase or release at the transition into the manic states, as established in the previous case. Special tests relating to the water and salt metabolism were, however, carried out whilst the patient was at rest and after fluid and salt intake had been stabilised for a long period.

1. *Water Test.*

Three pints of water were given on an empty stomach at 7 a.m. and the water output was checked hourly for 12 hours. In five tests performed in different cycles in each of the two experimental periods, the peak of urinary output occurred regularly in the second collection in the manic phase. In the depression this was the case in two tests only, while in the remaining three peak was reached in the third collection. In mania, increased output and dilution of urine invariably began in the first hour, whereas in the depression this occurred only in two tests.

2. *Pituitrin Test.*

Three pints of water were given and at the same time 10 units of pituitrin were injected; following this, the procedure was the same as before. Seven such tests were carried out in manic and six in depressive phases. As Graph II shows, the diuresis and dilution of urine began in the manic phase not later than between the fourth and fifth hour, and reached its peak two hours later, whilst in depression, the corresponding points were reached at least one hour later.

3. *Salt Test.*

Salt (10 gm.) was administered with the usual quantity of fluid at breakfast (300 c.c.), the urine collected at two hours' intervals, and the volume, specific gravity and chloride determined. Five tests in the manic phase and four tests in depression were carried out. It will be seen from Graph III and IV that in the manic phase, maximal salt and water excretion with values from 3 to 5.7 gm. chloride and 250-360 c.c. of water per two hours appear regularly in the first four hours, whereas the respective values in the depression at the same period are 1.6-2.8 gm. chloride and 150-200 c.c. of water two hourly. Only once did the total output of chloride for 12 hours of the depression equal the lowest output in the manic phase. The excretion of water within 12 hours showed a maximum of 1,000 c.c. in depression and varied between 1,120 and 1,680 c.c. in the manic phase. Similar results were obtained when 10 gm. salt were given with 3 pints of water in two depressive and two manic phases. Total outputs in the manic phase in 12 hours were 2,520 and 2,550 c.c. of water and 13 and 19 gm. chloride respectively, and in the depressive phase the corresponding figures were 1,630 and 1,850 c.c. of water and 8 and 10.7 gm. chloride. The proportion of the total outputs in the first hours was much greater in the manic than in the depressive phase.

The results of these different tests are in good agreement, and it is evident that under standard test conditions there is during the depressive phase a delay in the excretion of salt and water relative to that in the manic phase.

COMMENT.

Retention of urine in depression has been mentioned in the earlier literature (Lange, 1928), but no data of water intake and output were recorded. Hoff and Pötl (1930) studied in a number of manic-depressives the diuresis in the depression after the ingestion of water and found, in the majority of their cases, delayed excretion; they also found that neither antidiuretics (pituirrin) nor diuretics had any effect upon the diuresis in depression. Thorvardsson (1942) administered in 9 cases of depression 1,000 c.c. of water and found the output much delayed; but when the same patients took 1,500 c.c. of water for two days prior to the test the water excretion test became normal. Recently Altschule and Tillotson (1949) reported retarded excretion after water ingestion (1,500 c.c.) in some of their depressed patients. The observations of Thorvardsson confirm investigations on salt and water metabolism (McCance, 1936; van Slyke and Peters (1931) which show that random water ingestion tests without strict control and without regard to previous salt and water intake are of doubtful value; such control is for obvious reasons specially indicated in manic-depressive illness. Under the conditions under which our patient was investigated this source of error can well be excluded. In the previous case retention of salt and water in the depression and their release occurred in spite of normal intake; this could not be established in the present case, possibly on account of the relatively long duration and irregularity of the two phases. There was, however, evidence, from the special tests applied, of salt and water retention in the depression as compared with the manic phase. In considering

the possible meaning of this finding, certain clinical features common to both cases might be of some significance. In both cases sleep was increased in the depression, and it was almost absent during the fully developed mania; increased sleep was therefore associated with salt and water retention and sleeplessness with their release. As to these two functions, the pattern in the depression corresponded in the previous case to a normal night pattern, the mania to the day pattern. The normal daily biphasic rhythm was thus replaced by a cycle determined by the duration of the manic and depressive phases. Though these relations are not so close as to salt and water excretion in the present case the tendency is indicated by the described tests. As the regulation of this diurnal rhythm is probably due to a common mechanism in which, considering clinical and experimental experience, the diencephalon seems to play an important part, the disturbance observed may be the result of functional disorder of this region. It might therefore be of some importance that the symptomatology was in both cases mainly of somatic nature, and that in the present case an excessive gain in weight was found in the final prolonged depression.

SUMMARY.

Clinical and biochemical investigations were carried out on a 44-year-old patient who for five years had short manic-depressive cycles. The biochemical results, specially considered in this paper, were retention of salt and water in the depression as compared with the manic phase. There was a concurrent tendency to prolonged sleep in the depression and sleeplessness during mania. This association was still more striking in a previous case, where the normal diurnal cycle of sleep-wakefulness and water and salt excretion was replaced by the manic-depressive cycle. A disturbance of a regulatory diencephalic mechanism was considered possible—a view which seemed to be supported by general features in the clinical picture of the two cases.

I should like to express my indebtedness to Dr. Hemphill for allowing me to investigate a case of his, and I wish to acknowledge the help rendered by J. J. Gordon, D.Sc., and E. R. Cook, B.Sc., in carrying out the biochemical investigations of urine and blood constituents.

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Part II.—Bibliography and Epitome.*

AN attempt is being made to provide as far as possible a complete bibliography compiled from journals dealing with Psychiatry and Neurology (which are really inseparable) and their ancillary subjects, psychology, anatomy of the nervous system, criminology, etc.

If any reader can add the names of journals to the following list, which it is hoped to publish each year in the January number, the addition will be gratefully received and acknowledged.

Those journals which are available in the Library of the Royal Medico-Psychological Association are marked "1," those available in the Library of the Royal Society of Medicine are marked "2," those in the Library of the British Psychological Society are marked "3," and those in the Library of the British Medical Association are marked "4."

The titles of these journals are mostly in the form given by the Board of Editors of Publications of the American Psychological Association, January, 1939. Contributors are requested to use the exact form given below.

PSYCHIATRIC JOURNALS.

- 2 *Abh. Neur. Psychiat.* (now *Biblio. Psychiat. Neur.*).
- Abh. Psychother.*
- 2 *Acta Luso-Española Neur. y Psiquiat.*
- 2, 4 *Acta Neurol., Naples.*
- 2, 4 *Acta Neurol. Psychiat. Belg.*
- 1, 2, 3, 4 *Acta Psychiat. et Neurol., Copenhagen.*
- 3 *Acta Psychol., Hague.*
- Acta Psychol., Keijo.*
- Alcohol Hyg.*
- Alg. Neder. Tijdschr. Wijsbegeert. Psychol.*
- 2 *Aliénist v. Neurologist.*
- Aliéniste Français.*
- 2 *Allg. Ztschr. f. Psychiat.*
- 2 *Altersprobleme.*
- Amer. Imago.*
- 1, 2, 4 *Amer. J. Ment. Def.*
- 1, 2, 3, 4 *Amer. J. Orthopsychiat.*
- 1, 2, 3, 4 *Amer. J. Psychiat.*
- Amer. J. Psychoanal.*
- 2, 3, 4 *Amer. J. Psychol.*
- 2 *Amer. J. Psychotherap.*
- Amer. Psychologist.*
- An. Bras. Hig. Ment.*
- An. Istit. Psicol. Univ. B. Aires.*
- 4 *An. Port. Psiquiat.*
- An. Psicotec., Rosario.*
- 2 *Anal. Inst. Neurol., Montevideo.*
- Analele Psihol. (Rumania).*
- Anales de psicol., Buenos A.*
- 2, 3 *Année Psychol., Paris.*
- 2, 3, 4 *Ann. Méd.-Psychol., Paris.*
- 2 *Ann. Osp. psichiatr., Perugia.*
- 2 *Appl. Psychol. Monogr., Washington.*
- Arb. Psychiat. Inst., Sendai.*
- 2 *Arch. Antrop. crim.*
- 2 *Arch. Argent. de Neurol.*
- Arch. Argent. Psicol. norm. pat.*

* A number of extracts in this section are reproduced from *Chemical Abstracts and Psychological Abstracts*. To the Editors of these two Journals we extend our grateful thanks.

- 2 *Arch. Bras. de Neur. e Psiquiat.*
Arch. Brasil Hig. Ment.
Arch. Chilenos de Crim.
Arch. Ital. di Studi Neuropsich.
 2 *Arch. Neurobiol.*
 2 *Arch. Neurocir., Paraguay.*
 2, 4 *Arch. Neurol., Paris.*
 2 *Arch. de Neurol. de Bucarest.*
Arch. de Neurol.
 2 *Arch. di Antropol. Crim.*
Arch. di Crim. Neuropsiquiat. y Disc. Con., Quito.
 4 *Arch. di Sci. Cereb. Psych., Salerno.*
 2, 4 *Arch. f. Psychiat.*
 2, 3 *Arch. ges. Psychol.*
 2, 4 *Arch. Internat. de Neurol.*
Arch. Ital. Psicol.
Arch. Ital. Sci. Neur.
Arch. Krim. Anthropol.
 1, 2, 3, 4 *Arch. Neurol. Psychiat., Chicago.*
Arch. Neur. Psychiat., Mex.
 2, 3, 4 *Arch. Psicol., Neurol., Psychiat. e. Psicoter., Milan.*
 2, 3 *Arch. Psychol., Genève.*
 2, 3 *Arch. Psychol., N.Y. (ceased publication 1945).*
Arch. Relig. psychol.
Arch. Speech.
 4 *Arch. Venez. Soc. Oto.-rino.-lar.-oft.-neur. Caracas.*
Arq. do Assist. a Psicop. de Pernambuco.
 4 *Arq. Assist. Psicop. Sao Paulo.*
 2, 4 *Arq. de Neuro-psiquiat., Brasil.*
 3 *Aust. J. Psychol. Phil., Sydney.*
- Behaviour.*
Beih. Schweiz. Z. Psychol. Anwend.
Beih. Zbl. Psychother.
Biblio. Psychiat. Neur.
Bol. Inst. Psiquiat., Rosario.
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- 1, 2, 3, 4 *Brain.*
 3 *Brit. J. Addiction.*
 3 *Brit. J. Educ. Psychol.*
 4 *Brit. J. Hypnot.*
 2, 4 *Brit. J. Inebriety (now Brit. J. Addiction).*
 1, 2, 3, 4 *Brit. J. Med. Psychol.*
 2, 3, 4 *Brit. J. Psychol.*
 2, 3 *Brit. J. Psychol. Monogr. Suppl.*
Bull. Canad. Psychol. Ass.
 2, 4 *Bull. de la Soc. de Psychiat. de Bucarest.*
 2 *Bull. de la Soc. Roumaine Neur. Psychiat. Psychol. Endocrin.*
Bull. du Group. Franç. d'étud. de neuro-psychopath. infant.
 2 *Bull. industr. Psychol., Melbourne.*
 2, 4 *Bull. Los Angeles Neurol. Soc.*
 2, 4 *Bull. Menninger Clin.*
Bull. Milit. Clin. Psychol.
Bull. Soc. Psihol. med., Sibiu.
- 4 *Canad. Journ. Occup. Ther.*
 4 *Canad. J. Psychol., Toronto.*
 2, 4 *Cervello.*
 2, 3 *Character and Per. (now J. Personality).*
 2 *Child Developm.*
 2 *Child Developm. Abstr.*
Child Developm. Monogr.
Child Study.
Chin. J. Educ. Psychol., Chungking.
Chin. J. Psychol.

- 3 *Comp. Psychol. Monogr.*
 2, 4 *Confinia Neurol.*
 Contr. del Lab. di Psychol.
 Contr. Lab. Psicol., Milan.
 Contr. psychol. Theor.
 4 *Criança Portuguesa.*
 Criminalia, Mexico.
- 2, 4 *Deutsche Ztschr. f. Nerven.*
 2, 4 *Dig. Neurol. Psychiat.*
 2, 4 *Dis. Nerv. Syst.*
- 3 *Educ. psychol. Measmt., Washington.*
 Egypt. J. Psychol., Cairo.
 2, 4 *Electroenceph. Clin. Neurophys., Boston.*
 1, 2, 3, 4 *L'Encéphale.*
 2 *Épilepsia.*
 2 *Evolut. Psychiat.*
 1, 2, 4 *Excerpta Medica, Sec. VIII, Neur. Psychiat.*
- Fiziol. Th. S.S.S.R.*
 2 *Folia Neuropath. Esthon.*
 2, 4 *Folia Psychiat. Neur. Neurochir., Amsterdam.*
 2, 4 *Folia Psychiat. et Neurol. Jap.*
 2 *Fortsch. Neur. Psychiat.*
- 2, 3 *Genet. Psychol. Monogr.*
 2, 4 *Geriat., Minneapolis.*
 4 *Giorn. di Psich. e di Neuropat.*
- 4 *Howard Journal.*
 1 *Hum. Factor.*
 2 *Hum. Relat., Cambridge, Mass.*
 2, 3, 4 *Hyg. Ment.*
- 4 *Illinois Psychiat. J.*
 2, 4 *Index Neurol. y Psiquiat., Buenos Aires.*
 Indian J. Neur. Psychiat, Calcutta.
 3 *Indian J. Psychol., Calcutta.*
 4 *Indiv. Psychol. Bull., Chicago*
 3 *Industr. Psychol.*
 3 *Industr. Psychotech.*
 1, 2, 3, 4 *Int. J. Psychoanal., London.*
 2, 3 *Int. Z. Psychoanal. u. Imago.*
- Jap. J. appl. Psychol.*
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 Jap. J. Psychol.
 1, 2, 3 *J. Abnorm. Soc. Psychol., Washington.*
 J. Amer. Soc. Psychic. Res.
 3 *J. App. Psychol., Washington.*
 2, 4 *J. Belge Neur. Psychiat (now Acta Neurol. Psychiat. Belgica).*
 4 *J. Bras. Neur., Rio.*
 2, 4 *J. Bras. Psiquiat.*
 2 *J. Child. Psychiat.*
 2 *J. Clin. Psychol., Burlington.*
 2, 4 *J. Clin. Psychopath., Montecello, N.Y.*
 2, 4 *J. Comp. Neur.*
 2, 3 *J. Comp. Physiol. Psychol., Washington.*
 2 *J. Consult. Psychol., Washington.*
 J. Crim. Law and Criminol., Chicago.
 2 *J. Crim. Psychopathol. [now J. Clin. Psychopath.].*
 2 *J. de Psychiat. Infant [now Zeit. f. Kinderpsychiatrie].*

- 3 *J. Educ. Psychol.*, Baltimore.
J. Except. Child.
- 3, 4 *J. Exp. Psychol.*, Washington.
- 2 *J. f. Psychol. u. Neurol.*
- 3 *J. Gen. Psychol.*, Provincetown, Mass.
- 2, 3 *J. Genet. Psychol.*, Provincetown, Mass.
- 2, 4 *J. Geront.*, St. Louis.
J. Juvenile Res.
- 1, 2, 3, 4 *J. Ment. Sci.*, London.
- 1, 2, 3, 4 *J. Nerv. Ment. Dis.*, New York.
- 1, 2, 3, 4 *J. Neurol. Neurosurg. Psychiat.*, London.
J. Neuropath. and Psychiat., Leningrad.
- 1, 2, 4 *J. Neuropath. Ex. Neur.*
- 2, 4 *J. Neurophysiol.*
J. Neuropsychiat. du Pacifique.
- 2, 4 *J. Neurosurg.*
- 3 *J. Parapsychol.*, Durham, D.C.
- 2 *J. Personality*, Durham, D.C.
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J. Psychol., Moscou.
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Investigations into the Colour-form Reaction of Epileptics.

The tendency to observe the colour rather than the form, or vice versa (colour-form reaction) of objects perceived has been the subject of a considerable number of investigations from the standpoints of genetic psychology and characterology. The influence of various mental disorders on this reaction hitherto has been investigated only in schizophrenics and epileptics—in the latter by means of the Rorschach method.

The present writer has studied the colour-form reactions of 213 epileptics ranging from 6-55 years of age and institutionalized at the State Institution for Epileptics, Vilhelmsro, Jonkoping, Sweden. Since colour-form reaction varies according to differences in intellectual level and constitutional type, both intelligence tests and the determination of constitution were undertaken, in addition to which a survey is given of earlier investigations in this field.

The I.Q. has been determined by means of "A Point Scale for Measuring Mental Stability," by Yerkes, Bridges and Hardwick, translated into Swedish by Wahlen. The mean I.Q. of the entire material was found to be 67.1 ± 1.5 .

The determination of constitution was carried out according to Stromgren on the adult epileptics, totalling 116 cases. Mean index = -0.9, i.e. a pronounced leptosome index. Only three patients showed a pyknic index.

The colour-form reaction was investigated with Lindberg's Ring Test, the resultant initial colour responses being distributed between different intelligence and constitution groups.

Initial colour responses were given by 49.1 per cent. of the female patients and 54.4 per cent. of the male patients (according to Lindberg's evaluation method, 60 and 67 per cent. respectively).

In the under eighteen age groups the material in the different intelligence groups is too scanty to permit of any comparison with Lindberg's material; but on the other hand a comparison is possible between the colour reactions of the adult epileptics (66.9 per cent.) and of Lindberg's surgical case material (21.5 per cent.). The difference amounts to 45.4 ± 2.7 per cent.

The leptosomatic epileptics exhibit a colour reaction 32 ± 6.7 per cent. higher than Lindberg's leptosomatic mentally-insufficient patients.

The marked tendency towards colour reaction of the epileptics is regarded by the author as a pathoplastic phenomenon, associated with the general "fall in level," as in the case of schizophrenics. (Author's abstr.)

The Duration of Experimental Disturbances in the Cerebrovascular Permeability Due to Circumscribed Gross Damage of the Brain.

Relatively gross damage was produced experimentally by electrocoagulation in a circumscribed region of the brains of rabbits and cats. The purpose in view was to determine the duration of the disorder in the vascular permeability subsequent to such injury. It was found that in the beginning a pronounced disorder of the vascular permeability was demonstrable. Later, during the first day after the injury an increasing stasis arose in the vessels in the centre of the lesion so that finally the vessels contained no circulating blood. On the other hand, in the peripheral area of the damaged zone there were passable vessels which showed evidence of a disorder in their permeability lasting as long as one week subsequent to the damage. The reason why this disorder should last so long is discussed, and it is suggested that this persistence might be due to a toxic lesion ascribable to autolytic processes.

In the present investigation no dural vessels growing into the brain scar were demonstrable, but the existence of such vessels in certain gross cicatricial formations in man is a well-known fact that may be of physiopathological importance not only mechanically but also from the point of view of permeability. If the experimental damage is infected so that abscesses develop, the perifocal disturbance in the vascular permeability will persist probably as long as the abscess lasts. In the authors' experiments the disturbance in the permeability was limited to the thin capsule of the abscess. (Authors' abstr.)

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A Statistical Study of Psychoses due to Drugs or other Exogenous Poisons.

1. Psychoses due to drugs or other exogenous poisons represent very few first admissions to hospitals for mental disease in New York State. Such psychoses average only about 0.2 per cent. of all first admissions.

2. Despite the small number of such first admissions, it is evident, nevertheless, that psychoses due to drugs, etc., are more frequent among females than among males.

3. Very few cases of such psychoses arise from poisoning due to a metal or to a gas. The largest simple category is probably that arising from the use of opium or its derivatives.

4. The average age of first admissions with psychoses due to drugs, etc. is approximately 46 years. Females averaged about a year older than males. Approximately 60 per cent. of such admissions are found within ages 35 to 54.

5. There was a high percentage of intemperate users of alcohol among first admissions due to drugs, etc.

6. When classified as to marital status, all first admissions with drug psychoses, etc., except the married group, were in relative excess of the numbers expected when compared with similar marital groups in the general population. The excess was especially marked among those who were separated or divorced.

7. When compared with the general population, first admissions with drug psychoses, etc., did not show any significant differences with respect to degree of education. However, they included higher percentages with a high school or college education than is found among all first admissions.

8. Psychoses due to drugs, etc., occurred more frequently among the urban than among the rural population. With respect to the latter, they were confined to the non-farm group.

9. Negroes had a higher rate of first admissions with drug psychoses, etc., than whites. This was due to a great excess among Negro males. Negro females on the contrary contributed less than their quota of such first admissions.

10. Foreign-born whites had less than their quota of first admissions with psychoses due to drugs, etc. Native whites had an excess of such admissions.

11. There is a suggestion of a relatively high rate of first admissions with psychoses due to drugs, etc., among Jews, in contrast with unusually low rates of first admissions with alcoholic psychoses among them. (Author's abstr.)

Wave and Spike Discharges in the EEG.

The wave and spike formations occur usually on the background of a normal basic cortical rhythm, are remarkably constant in their occurrence in a frequency range of 2.5-3.5 cycles per second, but show considerable variations in the position and amplitude of the spike component in the same record, and indeed within the same discharge. The wave and spike formations are seen most frequently during hyperventilation. Other paroxysmal disturbances occur in 50 per cent. of the records, and the most frequent of these are single or multiple spiking discharges and paroxysmal bursts of 4-6-per-second activity. A surprisingly high incidence of wave and spike formation occurs after the age of 30 years. (Authors' abstr.)

Involuntional Melancholia and Convulsive Therapy.

Results of 61 involuntional cases discharged from the Institute of Living, 1935-37, prior to convulsive therapy, are compared with those of 347 involuntional cases treated with convulsive therapy between 1945 and 1947. The average number of electric treatments for melancholia cases was 10.8; for paranoid cases 16.2; for mixed cases 11.8. In both series of pre-shock and shock eras, the patients benefited from estrogen therapy and the re-educational and vocational programs, the latter with progressively increased facilities.

The average duration of hospital stay was $1\frac{1}{2}$ years in the pre-shock era as compared to 6 months with convulsive therapy.

The combined percentage of patients recovered and improved was essentially the same in both series (92 per cent. in 1935-37 and 90 per cent. in 1945-47). However, in the pre-shock era, 30 per cent. of melancholia cases were considered as recovered as compared to 62.5 per cent. of those receiving convulsive therapy; 62 per cent. were considered as improved as compared to 27.5 per cent. with convulsive therapy. The criteria of recovery not being the same in both series, these latter figures cannot be compared without reservation. However, even allowing for the difference in criteria of what constitutes recovered, there is material evidence to indicate that the shock-treated group left the Institute in better condition than the non-shock group. On the other hand, there is conclusive evidence that the length of stay in the combined recovered and improved group was materially shortened. The non-shock-treated group remained in the Institute on an average of three times as long as the shock-treated group. This difference in the length of hospitalization can hardly be accounted for by the improved and increased ancillary therapies which had undergone considerable development with the shock-treated group. (Author's abstr.)

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Electroencephalographic Effects of Bilateral Prefrontal Lobotomy.

1. A selected group of 25 chronic psychiatric cases who manifested seizures after lobotomy and 46 chronic psychiatric cases who were seizure-free after lobotomy were studied clinically and electroencephalographically.

2. An analysis of the prelobotomy EEGs of the seizure and seizure-free group revealed only slightly increased abnormality in the seizure group (33 per cent. as compared to 24 per cent.), more slow dysrhythmia in the seizure group, and more fast dysrhythmia in the seizure-free group.

3. Considering only the cases who had electric shock treatments before lobotomy, those in the seizure group averaged approximately twice as many treatments as those in the seizure-free group (31 as compared to 15). However, the difference in amount of shock treatments given to the two groups was not reflected in the prelobotomy EEGs.

4. Immediately after lobotomy almost all patients exhibited a drowsy akinetic state accompanied by diffuse slow potentials of increased amplitude. When the patients were aroused by means of various types of stimuli, the slow waves in the posterior leads were temporarily replaced by alpha rhythm, but slow activity in the anterior leads remained. As the akinetic state gradually subsided, the occipital slow waves were replaced by normal alpha rhythm, but the frontal slow activity persisted for a longer period of time.

5. Following lobotomy, there was an extremely high incidence of very slow "rolling activity" which was observed in frontal, precentral, and to a lesser extent in motor and temporal leads.

6. Slow activity from leads about the injured area was at its height within the first two weeks after lobotomy and then began to decline. This decline was well marked in the seizure-free cases, but in the seizure cases slow wave abnormality tended to persist.

7. One month or more after lobotomy the incidence of abnormal EEGs was much higher in seizure cases than in seizure free cases (76 per cent. as compared to 38 per cent.).

8. One month or more after lobotomy the incidence of focal EEGs was much higher in seizure cases than in seizure-free cases (41 per cent. as compared to 12 per cent.).

9. EEG abnormality in the seizure cases was in part dependent upon the interval between the seizure and the recording of the EEG. When the interval was short (days), the EEG was usually more abnormal than when the interval was long (months or years). However, the majority of EEGs recorded more than one year after a seizure were still abnormal.

10. Clinical analysis of cases with postlobotomy seizures revealed the following:

(a) The interval between lobotomy and onset of seizures varied from days to years, with a peak at 3 months to 1 year.

(b) During a follow-up period varying from 3 months to 4 years, the majority of patients experienced only 1 or 2 seizures. However, some patients had frequent convulsions, and status epilepticus occurred in 2 cases.

(c) In the large majority of cases, attacks were of the *grand mal* type. Two

patients had Jacksonian seizures in addition to *grand mal*, and 2 patients had tonic seizures. No *petit mal* or psychomotor seizures were observed.

11. Postlobotomy seizures did not negate the beneficial effect of lobotomy upon the mental disorder. The clinical follow-up study after lobotomy revealed that the seizure cases were doing as well as, or better than, the seizure-free cases.

12. There was no correlation between EEG findings (either before or after lobotomy) and the beneficial effect of lobotomy upon the mental disorder.

13. There were 4 patients with severe chronic postlobotomy headaches, all of whom had abnormal focal EEGs in addition to postlobotomy seizures.

(Authors' abstr.)

Experimental Observations on the So-Called Senile Changes of Intracellular Neurofibrils.

Various observations reported in the literature suggest that the so-called Alzheimer changes of the intracellular neurofibrils in senile and presenile conditions are associated with dehydration.

In the present experiments rabbits' brains were dehydrated *in vivo* by intravenous administration of 25 per cent. glucose solution. Microscopic examination showed that in some nerve cells, irregularly scattered in the brain, the intracellular argentophile fibres become coarse, and have a tendency to become matted strands. The nucleus remains intact. These changes correspond to the initial stages of Alzheimer's cell change in man as encountered in senile and presenile conditions. These findings are discussed in the light of the literature on this subject.

The histological findings in experimental hydration are also reported.

(Authors' abstr.)

A Comparison of the Test Performances of the Brain-Injured and the Brain-Diseased.

This paper is the fourth in a series dealing with encephalopathy due to brain injury and brain disease. The test results indicate that the functioning and efficiency of the patients in both groups follow a similar pattern: Full-scale I.Q.'s within the normal limits, verbal scores significantly higher than performance ratings, and low inter-group differences for full-scale, verbal and performance scales. The brain-injured patients on the average, showed more marked discrepancies between the verbal and performance subtests. The functions that are impaired or inefficient are discussed. The author holds that the statistical findings do not fully justify the quantitative interpretation that such rigid constructs as mathematical limits would imply. The effects of an encephalopathic process are serious, but an unmeasurable consideration must be given to the impact upon the personality structure of the patient. It is questionable whether any statistical technique exists at present which could factor out this pervasive element satisfactorily.

A comparison of the performances of both groups on the Bellevue Intelligence Scale shows similar function losses in addition to a consistent mean subtest weighted score pattern. For those interested in designing scatter-patterns the procedure suggested previously still holds: Use information weighted score as the basal point for deviation computation of the other 10 subtest weighted scores. The order of deviation of these 10 subtests from information—from most to least deviated—is: Digit symbol, digit span, block design, object assembly, and picture arrangement.

(Author's abstr.)

A Psychometric Determination of Alcoholic Addiction.

There is a need for an objective test to identify the alcoholic addict. Such a test undoubtedly would conserve personnel and time within large screening programs. In clinical practice, such a test might be valuable as a therapeutic device.

A 60-question test, called the Alcadd Test, was constructed and used. In the present study, 123 alcoholics were compared with 159 nonalcoholics on the Alcadd Test. The 2 groups were relatively comparable in age, intelligence and socioeconomic status. Illiterates, mental defectives, psychotics and deteriorated individuals were not used.

The following conclusions have been drawn:

1. A paper-and-pencil test, simple to administer, score, and interpret has been found useful in the identification of the alcoholic addict.

2. Highly significant statistical differences in mean scores on this test were found to exist when alcoholics were compared with social drinkers and abstainers. Significant differences also were found when social drinkers and abstainers were compared.

3. The Alcadd Test made approximately 97 per cent. correct predictions of alcoholics and 94 per cent. correct predictions of social drinkers. It predicted 100 per cent. correctly for the abstainers.

4. Using the shorter approximation of the Richardson-Kuder formula, a coefficient of reliability of .92 was found for the males and .96 for the females.

5. A subjective analysis of the 60 items on the Alcadd Test revealed 5 characteristics of the alcoholic addict. They were as follows: (a) Regularity of drinking, (b) preference for drinking over other activities, (c) lack of controlled drinking, (d) rationalization of drinking and (e) excessive emotionality.

6. Male alcoholics appear to be more consistent drinkers and show stronger preferences for drinking than do female alcoholics. Female alcoholics show much less control over their drinking, more rationalizations for their drinking and more emotional immaturity than male alcoholics.

7. Abstainers consistently make lower scores on the 5 alcoholic characteristics than do both alcoholics and social drinkers.

8. The Alcadd Test can be completed in less than 10 minutes and scored in 2 or 3 minutes. A profile of the 5 traits can be immediately constructed.

(Author's abstr.)

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Presenile Sclerosis (Alzheimer's Disease) with Features Resembling Pick's Disease.

Two cases of presenile dementia are presented. In each of these cases the brain manifested pronounced focal atrophies affecting chiefly the temporal lobes, in addition to generalized atrophy of the cerebral cortex. Histologic examination revealed the presence of numerous senile plaques and neurofibrillary changes throughout the cortex. Concomitant with these typical Alzheimer features were focal accumulations of inflated cells limited to the focally atrophic gyri and sparing the precentral, postcentral, transverse, temporal and occipital gyri. These inflated cells as seen in Nissl sections were ballooned cells with clear cytoplasm and an eccentric nucleus. Silver stains disclosed that they were not morphologically uniform but were in various stages of degeneration. Some contained argyrophil inclusions which made them resemble the cells of Pick's disease. Others had cytoplasmic structures which appeared transitional between neurofibrillary degeneration and the argyrophil bodies. Finally, some had a clear, unstained cytoplasm in both Nissl and silver preparations.

These cases were unique in that they were characterized by typical changes of presenile sclerosis concomitant with inflated cells similar in appearance and distribution to those seen in Pick's disease. The presence of intermediary forms linking the fibrillary cytoplasmic changes with the argyrophil suggests that they may be phases of the same degenerative process. Furthermore, the inflated cells as seen in Nissl sections may be morphologically variable, for silver methods revealed that some contain argyrophil bodies and others showed only a clear, unstained cytoplasm.

From these cases and others described in the literature, there is evidence of considerable variability in the presenile degenerations known as presenile atrophy

(Alzheimer's disease) and Pick's disease. There may be conditions which are intermediate between the two diseases. (Author's abstr.)

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Relation of Changes in Carbohydrate Metabolism to Psychotic States.

A study was made of the possible effect of changes in the mental status on the glucose tolerance (Exton-Rose technic) in 28 patients, (11 men and 17 women). The agent used to produce the psychiatric changes was electric shock therapy. A variety of psychotic types were investigated, the commonest classification being schizophrénia (16 cases).

In the majority of cases the glucose tolerance as a whole was little affected by the degree of improvement shown, but in individual cases there was a notable relation between the emotional disturbances and the response to sugar. This relation was due not to the presence or absence of psychotic manifestations but to the underlying residue of emotional tension. Only those patients who had apparently made some solution of their problems showed a "normalizing" of their glucose tolerance. It is concluded that the decrease in the glucose tolerance which is commonly seen in psychotic patients is primarily due to the anxiety underlying the mental disturbance. (Authors' abstr.)

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The Superiority Attitude and Rigidity of Ideas.

The superiority complex is described as a more or less completely developed trend toward a secure and gratifying, even exalted, self-estimation. A certain uniformity of personality traits is detectable, and an attempt is made to delineate them as a type. Any disruption of the superiority feeling is exceedingly painful, and the possessor, therefore, is distinguished by his inability to adapt himself to discordant realities. As a protection against these realities, he is totally committed to a fixity of views that will afford absolute security. These rigid formulations pervade the entire mental life. In the effort to eliminate uncertainties, a cosmology of cause and effect relations approaching the metaphysical may be constructed, while efforts to control events may show magic components.

Psychoneurotic phenomena appear when the superiority system has been breached by the impact of the circumstances. The simplest is the anxiety-depressive reaction, indicating the direct reaction to the imminence of psychic pain. More spectacular, however, are the obsessions and compulsions, in which protection is achieved by one's accepting the offending agent into consciousness only in the form of a symbol, thus permitting its vicarious destruction.

It is suggested that involutional depression arises from external trauma to some phase of the security organization, with complete failure of all protective mechanisms. An explanation is offered for the rapid spread of the depression to involve every aspect of the personality. (Author's abstr.)

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Analysis of a Prefrontal Lobe Syndrome and its Theoretic Implications.

The study reported has emphasized the importance of a severe limitation in associative range as a determinant of the behavioral disturbance after damages of the prefrontal regions. The hypothesis is offered, on the evidence from this case study, that symbolic activity is affected after damage to the prefrontal lobe because of the diminution in ability to shift from one associational trend to another. It is considered possible that the limitation of associations and the ensuing degradation of behaviour are dependent on the failure of symbols as links with or pivots for related experiences. Although it has been clear that lesions producing aphasia disrupt symbolic activity at more primary level, the limitation of associative range and of the use of symbols following lesions of the prefrontal regions has not been so apparent. Such limitations may not be noted readily both because of the diversity and breadth of human facilities, and because the limitations are masked by knowledge and behavioral patterns acquired prior to damage to the brain. In some cases, as in F.'s, the intellectual defect is obvious. In other cases in which the impairment is slight, little may be noted other than some degree of short-sightedness—an absence of consideration of the total circumstances and prior experience. As stated by Freeman, the thinking is finished more quickly and with greater satisfaction and assurance than in normal persons. In all cases of dysfunction due to lesions of the prefrontal lobes it may be that symbols, although readily available, are deprived of their full associative value, and that this limitation may affect the ability to utilize other assets. (Author's abstr.)

Combined Lateral and Ventral Pyramidotomy in Treatment of Paralysis Agitans.

1. A new surgical technique for the treatment of paralysis agitans is presented. In this procedure, combined lateral and ventral pyramidotomy, the lateral pyramidal and the opposite ventral pyramidal tract are sectioned through a single incision in the cord.
2. Use of this procedure in the treatment not only of tremor, but of rigidity and poverty of movement as well, is demonstrated in a series of 11 cases.
3. One case is presented in which combined lateral and ventral pyramidotomy was performed bilaterally, with good result.
4. Application of this procedure to the treatment of the major symptoms of paralysis agitans affecting one side or both sides is discussed. (Author's abstr.)

Plasma Calcium Fractions after Electric Convulsion Treatment.

Plasma calcium levels determined immediately before and immediately after an electrically induced *grand mal* convulsion showed an increase after the convulsion in each case, the average increase being 15.2 per cent. The initial increase in the total calcium of the plasma immediately after the convulsion was followed by a gradual decrease, which varied with the patient, and the preconvulsion calcium level was reached in all cases within 90 minutes after the convulsion.

The aforementioned increase in total plasma calcium after the convulsion may be attributed to an increase in the non-ultrafiltrable calcium fraction (largely protein-bound calcium); the ultrafiltrable calcium fraction remained essentially the same before and after the convulsion. Plasma protein levels were also increased immediately after an electric convulsion treatment, and the electrophoretic patterns of the plasma of one patient under the same conditions indicated that within the limits of experimental error, all fractions of protein were increased proportionally.

Hematocrit determinations on the blood of 5 patients showed an increase in the ratio of red blood cells to plasma in each case. An average decrease of 10.9 per cent. in circulating plasma volume was found.

It seems that hemoconcentration occurs after an electrically induced *grand mal* convulsion, thus accounting for the reported increase in several constituents of the plasma. However, some other mechanism may operate to account for the fact that the plasma calcium fractions do not increase proportionally after the convulsion. (Authors' abstr.)

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Effects of Ultraviolet Radiation on the Exposed Brain.

The recent introduction of ultraviolet radiation for antibacterial purposes has led to its use on the exposed human brain during neurosurgical procedures. Since the need for antisepsis is more important in the longer neurosurgical procedures, the necessity of knowing the prolonged effect of radiation on the exposed animal brain seems to be of immediate importance.

Ten cats were subjected to bilateral craniotomies. Ultraviolet radiations, having 80 per cent. of their wavelengths in the vicinity of 2,537 angstrom units, were allowed to project on to one hemisphere for five hours, while the other hemisphere, used as a control, was shielded from the radiations. Pathologic studies were made after the animals were killed, on the third, fourth or fifth post-operative day.

Exposure of the cat brain to ultraviolet radiation under actual human operating conditions produced dilation of meningeal and cortical vessels, usually within 30 to 60 minutes. Gross congestion subsided in 20 minutes by elimination of the ultraviolet radiation. Re-irradiation, however, provoked a rapid redilation.

Petechial hemorrhages were observed on the irradiated side in all animals at autopsy, on the third or fifth post-operative day. In one animal cortical petechiae were already visible towards the end of the five-hour exposure.

On inspection of the exposed cortex slight edema was suspected in only a few instances on the irradiated side. It was difficult to evaluate and recognize during exposure. However, in all the cases gross edema was observed at autopsy and was greater on the irradiated side.

Cortical electrograms were taken throughout the exposure in 4 animals. In 3 experiments depression of activity occurred after an exposure of one hour. In one animal epileptiform spikes developed after one hour, and this animal had a clinical seizure at the end of five hours. The electrographic alterations supervened during the stage of vascular congestion.

An intense inflammatory response was observed in the irradiated area. This consisted of vascular congestion of meningeal and cortical vessels; transudation of serum; cellular exudate, with cuffing of vessels; diapedesis, and numerous petechial hemorrhages.

Within the irradiated hemisphere ganglion cells were reduced in number, showed swelling and disruption of cell membranes and occurred as pyknotic forms in the more superficial layers.

Fibrous astrocytes showed evidence of mild hyperplasia of their projections on the irradiated side. The oligodendroglia remained normal, except about cysts and hemorrhages, where acute swelling occurred. The microglia was reactive, especially in the plexiform layer over the irradiated hemisphere.

It is concluded that prolonged ultraviolet irradiation of the brain is harmful and that further investigation is necessary to establish how long the brain may be irradiated without showing irreversible pathologic effects. Physiologic and electrographic observations during ultraviolet irradiation of the exposed brain suggest that with frequent irrigation of the brain, exposure of 30 to 45 minutes will not result in permanent harmful effects. (Authors' abstr.)

Electroencephalographic Changes after Prefrontal Lobotomy, with Particular Reference to the Effect of Lobotomy on Sleep Spindles.

1. Patients with lobotomy have generalized slowing, most prominent in the frontal leads, in the first few post-operative days. Slowing decreases in degree and extent slowly in the group, abruptly in individuals, and there is little change after three months.

2. The commonest long term electroencephalographic residuum of lobotomy consists in $\frac{1}{2}$ to 1 per second base line sway with normal frequencies superimposed.

3. Runs of 12 per second waves in sleep are most prominent in anterior leads before operation and virtually do not occur after lobotomy. It is assumed that they originate in the nucleus centralis medialis of the thalamus and that their absence in all leads after operation is due to degeneration of this nucleus.

4. Runs of 14 to 15 per second waves in sleep are most prominent in central leads before lobotomy, are more frequent in central leads and are less frequent in frontal leads after than before lobotomy. It is assumed that they originate in the nucleus centralis lateralis of the thalamus. When they are still present anterior to the lobotomy incision, it must be assumed that severance of fiber tracts between the cortex and thalamus is incomplete. When they are absent in frontal leads and present in central leads after lobotomy, it must be assumed that thalamo-frontal fibers are completely severed (unless orbital fibers have been spared).

5. Persistence of normal alpha activity in the frontal leads of patients whose sleep records demonstrate complete severance of corticothalamic fibers casts serious doubt on the theory that alpha activity is maintained solely by thalamocortico-thalamic reverberating circuits. (Authors' abstr.)

The Phobic Syndrome: A Study of Eighty-Six Patients with Phobic Reactions.

This report on 86 patients with phobic reactions indicates that the phobic person is fundamentally apprehensive, with an overactive sympathetic nervous system and a cyclothymic make-up. He is usually too closely attached to one parent and has not entered into mature adult relationships with other persons, even though he may have married and become a parent. Having been brought up "soft" he reacts to the dangers of everyday living by acquiring protective phobic reactions. His fears are merely symptoms of an underlying neurotic state; therefore the treatment of an adult with phobias consists in emotional retraining and reconditioning of specific fears through psychologic re-education or brief psychotherapy. In order that he may reap the rewards to which his exceptionally good personality entitles him, a potentially valuable but immature person must be assisted to grow up, to assume an adult's place in society. To bring this about, he must be taught to accept no orders from unreasonable fears.

Psychologic re-education requires approximately two months of intensive treatment which should be followed by several months of medical supervision to make sure that the patient does not regress into phobic or other neurotic reactions. This follow-up treatment is important, since phobic patients have a tendency to mislead the physician in an attempt to escape further treatment by making the doctor think that they are more nearly well than they actually are. The physician must be sufficiently experienced not to be deceived by such a person, who is frequently a master in deception. As long as any phobia is active, the patient is not cured. (Author's abstr.)

Studies on the Occipital Lobe. (I) Significance of Small Areas of Preserved Central Vision.

Six cases of occipital lobectomy are presented in detail, and their results with regard to preservation of central vision are summarized.

The various theories advanced to explain macular sparing are discussed. Previous series of occipital lobectomy are reviewed with reference to the present status of the doctrine of cortical localization of the macula.

It is concluded that there is no evidence to support a theory of bilateral macular or foveal representation.

Preservation of central vision ranging from 0.25 to 1.5 degrees was observed in the authors' patients with occipital lobectomy. However, the same degree of macular sparing was found in eight control patients with chiasmal lesions. It was felt that the situation and extent of the lesion in the optic pathways, as well as a minimal eccentricity of the fovea with slight physiologic variation in fixation, explain the results most satisfactorily. (Authors' abstr.)

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Tridione Therapy in Minor Epilepsy.

Tridione has been satisfactory in the treatment of minor epilepsy in 38 out of a series of 45 cases. In 12 the attacks were abolished and in another 15 almost complete control was achieved. In 13 further cases there was a significant reduction in the incidence of attacks.

Of the remaining five cases three showed slight improvement. Two failed to respond.

Five patients with psychomotor epilepsy were made worse by tridione.

Minor side-effects—photophobia, mild sore throat, a few papules on the face, chest or arms—were not uncommon. In two patients there was an urticarial reaction which subsequently developed into generalized exfoliative dermatitis necessitating discontinuation of tridione. In a third case treatment was temporarily discontinued following the appearance of facial erythema and oedema. At a later date tridione was successfully used in these three cases without harmful effects.

Apart from transient eosinophilia in four patients the authors observed no significant alteration in the leucocyte counts.

The authors conclude that tridione is the most effective substance as yet available for the treatment of minor epilepsy. Although serious toxic reactions sometimes occur, they are not common and in hospital out-patient practice tridione is the drug of choice in the treatment of minor epilepsy. (Authors' abstr.)

The Orbital Gyri.

(1) The functions and connections of the orbital gyrus have been studied in a series of cats, dogs and monkeys.

(2) Electrical stimulation of the orbital gyrus affected blood pressure and respiration, the effects varying with the anaesthesia, the frequency of the stimulus, and the wave form of individual current pulses.

(3) Blood pressure and respiratory effects were obtained independently.

(4) The excitable area for these various autonomic responses corresponds to Area 13 of Walker, or "FF" of von Bonin and Bailey, and within this area there are discrete foci of maximal sensitivity.

(5) Stimulation of the anterior perforated substance is usually followed by a rise in blood pressure and respiratory arrest, as well as pupillary dilatation.

(6) Varying the frequency or the stimulus in the orbital gyrus and in the anterior perforated space may reverse the blood pressure reaction.

(7) Dilatation of the pupil eye movements, salivation, lacrimation and coarse motor movements were obtained by stimulation of the orbital gyrus and the anterior perforated space.

(8) The blood pressure and respiratory responses could be obtained after section of both vagi, the splanchnic nerves, and after removal of the adrenals, and destruction of both paraventricular nuclei of the hypothalamus, and after paralysing doses of tetra-ethyl-ammonium chloride.

(9) No suppression of somatic movements or of ECG could be obtained.

(10) Strychnine neuronography demonstrated connections to both homolateral and contralateral putamen, contralateral caudate nuclei, corpus callosum, H Field of Forel, median forebrain bundle, and lateral preoptic area, as well as the contralateral orbital gyrus.
(Authors' abstr.)

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Rhythmic Electrical Activity from Isolated Cerebral Cortex.

Bremer has demonstrated that rhythmic activity of the cerebral cortex, similar to the alpha rhythm, represents an inherent property of the cortex itself. In spite of Bremer's findings there has been considerable disagreement as to whether the rhythmic cortical activity depends upon the interaction of the cortex and subcortical structures, or whether the cortex is able to produce spontaneous rhythms.

Spontaneous and induced cortical activity has been investigated in cats in intact hemispheres, in hemispheres after thalamectomy, and in portions of the cortex which have been completely isolated from the rest of the brain.

Both after thalamectomy and after severance of all subcortical and intracortical connections to a small portion of the cortex, spontaneous rhythmic cortical activity was recorded, resembling the normal alpha rhythm.

Electrical activity induced by electrical or chemical stimulation in such preparations was indistinguishable from activity induced by the same means in normal hemispheres.

The results of this study give support to Bremer's views on the origin of the rhythmic cortical activity, and have led to the following conclusions:

1. Rhythmic electrical activity, closely related to the alpha rhythm, is an inherent property of the cortex itself. It is not necessarily dependent upon thalamo-cortical circuits, though these circuits, when present, may modify its form and amplitude.

2. The explanation of contradictory results obtained by some authors may be due to conditions of the cortex following operative procedures. The facility with which the effect of such procedures can be reversed by chemical stimulants like eserine and acetylcholine should be emphasized.

3. Rhythmic electrical activity in response to electrical or chemical stimulation of the cortex has the same characteristics in an isolated portion of the cortex as in normal cortex with intact connections, under the conditions of the authors' experiments. (Authors' abstr.)

The Electroencephalogram following Occipital Lobectomy.

The electroencephalograms of six patients whose entire left occipital lobe has been removed at operation have been reported.

Three abnormalities have been observed: (a) Diminished alpha activity in the left occipital area; (b) the occurrence of sharp waves and fast beta activity in the temporal, central and frontal areas; (c) over-activity of the left temporal lobe with the presence of abnormal waves, increased alpha-like waves and large voltage sleep waves. It is suggested that some of the increase in activity is probably the result of scar tissue. Although it is possible that some of the remaining irregularity might be the result of anatomical changes resulting from operation, it is suggested that there is some evidence that the increased activity represents a release phenomenon; (d) it is concluded that following complete removal of the striate area, the remaining portion of the hemisphere, especially the temporal lobe, is capable of generating an alpha-like rhythm. (Authors' abstr.)

Electrographic Study of the Convulsant Action of Intravenously Administered Acetylcholine.

1. Intravenous administration of large doses of acetylcholine induces convulsive respiratory movements, occasionally followed by tonic spasm of the limbs and tremor. In only one case a convulsive seizure clinically similar to a strychnine tetanus was observed.

2. Injections of convulsant doses of the drug induce arrest of the heart, which is followed by flattening of the cortical potentials and by spinal hyperactivity.

3. The changes in the electrical activity of the central nervous system evoked by intravenously administered acetylcholine are similar to those induced by asphyxiation.

4. It is concluded that the convulsive movements resulting from intravenous administration of acetylcholine are not of cortical origin, and that the hyperactivity of the spinal cord is probably a consequence of the deficient oxygenation which follows the circulatory changes induced by the drug. (Authors' abstr.)

Influence of Ammonium Chloride on the Electrical Activity of the Brain and Spinal Cord.

1. Intravenous injections of suitable doses of ammonium chloride in lightly anaesthetized dogs evokes various circulatory effects which may be only slight or sufficient to stop the heart altogether with conspicuous drop of the general blood pressure.

2. The occasional changes in the electrical activity of the cerebral cortex following the administration of the drug are probably a consequence of these circulatory changes.

3. Intravenous as well as local administration of ammonium chloride induces modifications of the spinal cord activity, which are probably independent of circulatory changes and consist of a simple activation or of an activation accompanied by synchronization of the spinal rhythms.

4. The activation accompanied by synchronization induced in the spinal cord by ammonium chloride resembles in many respects the spinal activation following strychnine administration, and possibly is due to increase in the number of active neurones and in their degree of synchronization.

5. Ammonium chloride produces a marked potentiation of strychnine action on the brain and spinal cord.

6. It is concluded that ammonium chloride fits are not of the epileptic type. (Authors' abstr.)

The Electroencephalogram in Cerebellar Seizures.

1. The EEG recorded in a series of cats undergoing cerebellar seizures was not specific in type.

2. It was unlike the EEG accompanying clonic seizures elicited by cerebral stimulation.

3. Involvement of a specific limb in the slow march of the seizure was not accompanied by specific alteration of the EEG from either side of the brain.

4. The EEG during a cerebellar seizure was best described as an activation pattern, being made of low amplitude fast waves.

5. When tracings from the cerebellum were recorded, no alterations were observed during a seizure, but the type of apparatus used did not allow complete analysis of the waves out of the range of the ordinary frequencies of the EEG.

(Authors' abstr.)

Effects of Thalamic Stimulation in Unanaesthetized Animals.

A cinematographic analysis of the responses of cats to local stimulation of various portions of the thalamus and hypothalamus has been varied out with histological control and with electroencephalography correlation both during operation and post-operatively in an attempt to investigate further the hypothesis of a diencephalic origin for *petit mal* epilepsy. The results of this investigation may be summarized as follows:

(1) Electrical stimulation within the intralaminar nuclei of the thalamus, especially rostrally and bordering upon the dorso-medial and antero-medial nuclei,

produced a sudden arrest of responsiveness which the authors have called the "arrest reaction." During this arrest the animal would remain immobile, with no loss of tone, and failed to respond to usually effective stimuli.

(2) The "arrest reaction" would persist beyond the period of thalamic stimulation in the form of an after-discharge resembling very closely a *petit mal* type of seizure in man, including the slight twitching movements about the eyes and face so commonly seen in these attacks, and would cease abruptly.

(3) More intense and more rapid stimulation of the same regions producing the "arrest reaction" would produce first a *petit mal*-like attack followed by a major generalized convulsion or "*grand mal*" seizure.

(4) Electrocorticograms showed that stimulation of the intralaminar regions of the thalamus which produced a generalized recruiting type of control of the rhythmic activity of the cortex also produced the generalized changes in behaviour which the authors have termed the "arrest reaction." During the *petit mal*-like seizures a bilaterally synchronous 3 per second wave and spike discharge was recorded from the cortex and was associated with a similar type of wave form in the thalamus. During the *grand mal*-like attacks the electrocorticogram and electrothalamogram showed rapid high-voltage activity simulating closely the form of the EEG at the onset of such attacks in man.

(5) Autonomic system responses including a complex defensive pattern of behaviour with sham rage or a fear pattern associated with flight were reproduced particularly from the hypothalamus and occasionally from the overlying midline nuclei of the thalamus. These results corresponded closely with the detailed analysis of such responses as reported by Hess.

(6) Extrapyramidal types of movement such as tonic postural states, turning of the head and body, circling movements, alternating movements of a limb, and so forth were reproduced from what was presumed to be the thalamic or sub-thalamic extrapyramidal system. These results also correspond closely to those described by Hess.

(7) Control studies in which stimulation of sensory relay nuclei was carried out produced no such reactions but only responses which gave one the impression of a paraesthesia or of a reaction to a sensory stimulus. On no occasion was any loss in general responsiveness or change in emotional behaviour observed when stimulating sensory relay nuclei.

(8) It is concluded from observations in the cat that the diffuse thalamo-cortical projection system which the authors have called the *thalamic reticular system* has a very widespread and profound effect on behaviour as a whole and may be involved in the mechanism of *petit mal* and generalized convulsive seizures as seen in man.

(Authors' abstr.)

Changes in the Electroencephalogram following Administration of Mesantoin (Methyl-phenyl-ethyl Hydantoin).

Electroencephalograms were obtained before, during and after administration of mesantoin (methyl-phenyl-ethyl hydantoin).

Reversible changes were noted as follows :

Percentage.

Decrease in alpha rhythm	58
„ slow activity	38
Increase in fast activity	62
No change	12

The dose of the drug and duration of administration seemed to have the closest correlation with these changes. There was little or no correlation between the changes noted and the age, sex or race of the patient, or with the duration, severity, type or degree of control of the convulsive disorder.

The changes observed necessitate recognition that when mesantoin is being administered progressive clinical improvement may be associated with increasing abnormality in the electroencephalogram.

(Author's abstr.)

Continuous Measurement of Alveolar CO₂ Tension during the Hyperventilation Test in Routine Electroencephalography.

1. A method is described for automatic and continuous measurement of the alveolar carbon dioxide during the hyperventilation test in routine electroencephalography. It depends upon the specific absorption of infra-red by CO₂, as measured

by an infra-red analyzer (K. Luft) which transforms changes in absorption into deflections of a membrane-condenser. The CO₂ concentration is recorded through the EEG amplifier on the ink-writer tape, and it appears as an alternating voltage of 7 cycles per second, the amplitude of each cycle representing the instantaneous CO₂ concentration in the analyzer.

2. Using this method, 98 healthy flying cadets were tested during a routine three-minute hyperventilation. There was a wide distribution of hypocapnic levels reached, covering the range of 10–28 mm. of Hg. The median of CO₂ tensions after one minute was 22.5 mm., after two minutes it was 20.5 mm., and after three minutes, 18.5 mm. Hypocapnia persisted in each case for more than two minutes after "normal breathing" was demanded.

3. The first appearance of slow wave activity in the EEG occurred over a wide range of alveolar CO₂ tensions. Whereas a number of cases went as low as 10–15 mm. without exhibiting slow waves, others showed a response as high as 25–28 mm. Hg. when hyperglycemia was not assured. With a selected group of five subjects it was demonstrated that raising the blood sugar above 130 mgm. per cent. necessitated a lower CO₂ tension for the elicitation of a given slow wave response, as compared to the fasting state. The progress through the different degrees of slow wave build-up was accompanied by only slight changes in alveolar CO₂ tension. In half of the cases the transition from 5–8 per second activity to 2–4 per second activity occurred within a range of ± 1 mm.

4. The disappearance of slow wave activity after termination of hyperventilation generally occurred at a higher CO₂ level than that of its appearance during hyperventilation. In the mean, 2–4 per second waves disappeared at a tension 2.3 mm. higher and 5–8 per second waves required an increment of 3.2 mm. Persistence of slow waves beyond two minutes post-hyperventilation indicated that there was either a facile EEG response at a relatively high CO₂ level or an inadequate recuperation from a low CO₂ level. (Authors' abstr.)

Path of Current Distribution in Brain during Electroconvulsive Therapy.

When the minimal electric current necessary to produce a clinical *grand mal* convulsion is administered to the head of a corpse, the current does not travel in a spindle or "onion"-shaped pattern between electrodes, but travels principally along neuronal paths, concentrating in such structures as the corpus callosum and traversing both sides of the head even when one electrode is applied to the vertex and the other to the parietal region. The extent to which it invades structures relatively deep in the brain stem may be of clinical significance. (Authors' abstr.)

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Liver Function and Nutrition in Relation to Toxic Psychoses.

(1) Toxic psychoses on a nutritional basis may occur without any physical signs of vitamin deficiency.

(2) If nicotinamide therapy is started immediately after the onset of psychosis and adequate diet is restored, the response may be very rapid and dramatic.

(3) In cases of longer duration, response to nicotinamide may be slow or even not occur until the adequate and normal liver metabolism is restored and recovery may occur only after three or four months' treatment.

(4) Several patients recovered on general measures aimed at restoration of liver function without massive doses of nicotinamide.

(5) All of our severe cases of long standing showed an accompanying liver insufficiency and it was only after the improvement in the liver function that the patient's mental functions were restored to normal.

(6) In depressed patients with an accompanying nutritional deficiency, electric shock treatment is of no value until after the nutritional deficiency has been adequately corrected.

(7) Heavy insulin shock is definitely contraindicated in toxic psychoses of nutritional origin.

(8) Vitamins alone have no value in restoring severe cases to normalcy.

(9) We feel that the term "toxic psychosis" is misleading and a more descriptive term, "nutritional psychosis" would be more appropriate for psychosis accompanying deficiency diseases. (Author's abstr.)

Brief Stimulus Electric Shock Therapy.

(1) Brief stimulus therapy is electroconvulsive therapy by means of current so modified that the average electrical energy necessary for production of the seizure is very much less than that necessary with classic sine wave currents.

(2) The clinical improvement obtained by use of BST is at least as good as that produced by the classic type of current.

(3) The chief advantage of the use of BST is the marked diminution and, at times, complete absence of confusion associated with electric shock therapy.

(4) The disadvantage of the treatment with BST is the increase of fear engendered in the patient; this, however, can be readily controlled by the use of pentothal sodium before the treatment. (Author's abstr.)

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Experimental Radio-Necrosis of the Brain in Rabbits.

A single X-ray dose of 2,850 r, under the physical conditions that have been defined, will produce delayed irradiation-necrosis in the rabbit's brain after a latent period of approximately one hundred days.

The latent period is lengthened by reducing the dose to 2,440 r.

The initial histological changes consist of minute foci of haemorrhage and necrosis which are intimately related to the perforating vessels and, in particular, capillaries. Increase of capillary permeability accompanied the established lesion but was not demonstrated at earlier stages.

The lesions when once initiated, appear to extend rapidly and to progress to non-irradiated parts of the brain. They are characterized, in later stages, by pronounced gliosis and by progressive degeneration and sclerosis of the adjacent vessels.

The neurones are only focally and secondarily affected.

The meninges and their blood vessels are unaffected and the superficial parts of the cerebrum escape, although the cerebellar cortex may be extensively damaged.

(Authors' abstr.)

Clinical and Pathological Observations on Relapse after Successful Leucotomy.

Six patients are described in whom mental illness recurred some considerable time after apparently successful leucotomy and in whom the precise extent of the brain lesions was subsequently determined in the laboratory. Anatomical features of the six cases are discussed, together with those of other "psychosurgical" cases in the literature in which the extent of the lesion was determinable during life. Clinical features of the six cases are reviewed together with those of other relapsed cases in the literature of "psychosurgery" in which diagnostic details are available. The following conclusions are come to:

1. Many of the symptoms and syndromes characteristic of affective and schizophrenic functional psychoses can recur after practically complete isolation of the prefrontal cortex from its fibre connections. Some chronic schizophrenic symptoms, at least, can not only persist but can disappear and then recur after full bilateral prefrontal lobectomy. Many neurotic symptoms can recur after disappearance following removal of more limited amounts of prefrontal cortex.

2. The illness which recurs is practically always of the same type as the pre-operative one.

3. There are indications that the power of environmental influences for both good and ill may be augmented after the operation.

4. Case 1 also touches on the problem of localization in the prefrontal regions in relation to type of personality change and to creative ability.

5. The facts demand a generous conception of the degree of plasticity within both the abnormally and the normally functioning brain. (Authors' abstr.)

Observations on the Wave and Spike Complex in the Electroencephalogram.

The EEGs of 100 cases showing typical wave and spike complexes were examined. Seventy-five of the patients were aged from 5 to 20 years inclusive.

Normal alpha rhythm was seen in 88 cases. Apart from the wave and spike complexes, 58 records were otherwise normal. Abnormal rhythms seen are described.

In 80 cases the wave and spike complexes occurred without overbreathing, but in 20 cases they appeared only when the patient overbreathed.

Overbreathing was done by 82 of the patients, and 74 of these developed wave and spike complexes in relation to the overbreathing.

The effect of opening and closing the eyes was observed in all the 100 cases. In 8 cases wave and spike complexes followed opening, and in 15 they followed closing of the eyes. In 4 of these cases there was a response both to opening and closing movements. In 3 cases opening of the eyes was seen to inhibit an existing wave and spike outburst.

The average number of wave and spike outbursts in a record before overbreathing was between 3 and 4.

The wave and spike outburst might last for less than a second or be almost continuous for several minutes. The total average duration of a single outburst per record was 8 seconds.

The length of individual outbursts in a single record showed much variation, but in some cases there was a striking constancy of duration of the outbursts.

In 94 cases the wave and spike complexes were entirely generalized. In 3 cases localized as well as generalized outbursts were seen. In 3 cases the complexes were localized to the frontal regions only. No special clinical features distinguished the few cases in which localized outbursts occurred.

In most cases the wave and spike outbursts appeared abruptly and synchronously in all leads. The complexes themselves might be preceded and followed by a short burst of irregular waves, and there was then a tendency for the wave and spike complex to assume its characteristic form more rapidly and more clearly in the fronto-parietal regions. The wave and spike complexes tended to persist longest in the area in which they were first seen. In about 10 per cent. of cases the outburst was predominantly fronto-parietal, and in 5 per cent. or less it was predominantly occipital.

During long outbursts the wave and spike complex tended to decrease slightly in frequency.

Twenty-nine patients showed obvious clinical attacks of *petit mal* during the recording. All clinical attacks were associated with wave and spike outbursts,

and these were usually of longer duration than the average. The liability to clinical attacks seemed to be rather more closely related to the duration than to the number of outbursts in the record, but there was no constant relationship between the severity of the clinical symptoms and the extent of the EEG changes.

So-called "pyknolepsy" could not be sharply distinguished from *petit mal* by the EEG any more than it could by clinical standards.

The clinical response of cases of *petit mal* to treatment with "tridione" was not necessarily associated with parallel changes in the EEG.

A random 20 minutes EEG record is of limited value in assessing the frequency of attacks, prognosis or progress of a patient with *petit mal*. It may, however, have great diagnostic value in doubtful cases. (Authors' abstr.)

Psychiatric Changes Associated with Friedreich's Ataxia.

1. Some cases of mental disturbances in association with Friedreich's ataxia have been described. These comprise the rare form of great severity, characterized by paranoid feelings and outbursts of excitement, in addition to depressive and confusional states.

2. The association with epilepsy is discussed, and abnormal electroencephalogram findings are recorded. It is suggested that these may help to account for some features of the symptomatology in certain of these cases. (Author's abstr.)

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Pick's Disease.

1. Seven cases of lobar sclerosis are reported. They fall into anatomic groups :

(a) In one form there is marked focal cortical devastation with loss of nerve cells and axis cylinders. Remaining nerve cells are swollen and may exhibit eccentric nuclei and argyrophilic cytophilic inclusions. There is astrocytosis of the cortex, and isomorphous fibrillary gliosis of the white matter. Demyelination and reactive gliosis parallel each other in severity. Damage to subcortical centers is not prominent. This type generally affects polar regions, either of the frontal or temporal lobes.

(b) In the other group there is widespread gliosis, cellular and fibrillary, of the subcortex, out of proportion to demyelination of these areas. Cortical damage is less prominent; there are nonspecific alterations to the nerve cells. Subcortical centers are frequently involved, including degeneration of descending motor pathways. The atrophy is generally not polar in distribution. Disturbances in motor and sensory spheres are observed rather than in brain structures associated with "higher" mental processes.

2. The literature is reviewed, and reported cases classified according to the above grouping, where this is possible from the original author's description.

3. It is suggested that these two types of circumscribed cerebral atrophy have a different etiology. (Author's abstr.)

The Central Nervous System in Hepatic Disease.

1. The central nervous system in 8 out of 18 cases of severe liver disease revealed extensive alterations.

2. The changes involved all regions of the brain and consisted of nerve cell damage and widespread areas of demyelination.

3. The tissue alterations were predominantly perivascular in nature, suggesting a toxic etiology.

4. From a review of the literature and a study of these cases it is felt that the liver damage enables some endogenous toxin to reach the brain and produce the widespread damage.

5. Two cases are reported in detail.

(Author's abstr.)

Pathologic Changes in the Central Nervous System Resulting from Experimentally Produced Hyperpyrexia.

The brains of animals dying shortly after subjection to hyperthermia demonstrated hyperemia, edema, and an acute disease process of the parenchyma without signs of beginning repair.

The brains of the animal living for several months after subjection to hyperthermia demonstrated evidence of parenchymatous damage undergoing repair. Clinically, this group of animals showed no disturbance in motor function or behaviour. They appeared and behaved like normal animals.

The application of a frozen carbon dioxide temperature collar about the neck, in the manner described, did not lower the temperature of the head or prevent heat stroke.

(Authors' abstr.)

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*Excitability Cycle and Interaction in Geniculate-striate System of Cat. <i>Marshall, W. H.</i>	277

Effect of Curare on Cortical Responses Evoked by Afferent Stimulation.

1. Intocostrin and d-tubocurarine chloride are each able to block synaptic conduction in the central nervous system.

2. After conduction over sensory pathways is blocked, impulses are still propagated retrograde over the corticospinal tract.

3. Spontaneous cortical electrical activity does not persist after synaptic conduction in the central nervous system has been blocked.

4. Depression of synaptic conduction always requires doses greater than those required for blocking neuromuscular conduction. In cats with intermittent administration of small doses intravenously, a per kilo. dose of 10 to 15 times the usual clinical dose was effective in eliminating all cortical response to stimuli conducted over sensory pathways. Occasionally, much smaller doses sufficed.

(Authors' abstr.)

Unipolar Electromyograms of Normal and Denervated Human Muscle.

The form of normal human muscle action potentials obtained with a unipolar micro-needle electrode may be described as follows:

1. A negative spike of 2-3 msec. duration preceded and followed by a positive potential of variable size, form and duration, depending upon the position of the needle point relative to the conducted spike process in the muscle.

2. Prolongation, distortion and attenuation in voltage results from spikes derived from fibres at a distance from the needle point and are considered to be largely derivation artefacts.

3. Small fibre potentials may occasionally appear superimposed upon the negative spike potential due to imperfect fusion of the many fibre potentials making up the normal motor unit but the duration of a normal unit does not exceed 4-5 msec. These irregularities may also be considered derivation artefacts since slight movements of the needle point may result in their disappearance.

4. Other apparent "polyphasic units" are due to either grouped firing of several adjacent motor units or occasional repetitive firing of single units.

5. In muscles of the face and in certain portions of limb muscles, motor units appear to have a more complex organization with overlapping of the distribution of terminal axonal networks causing poorly integrated multiple fibre potentials to appear.

6. Action potentials from single denervated muscle fibres during spontaneous fibrillation are characterized by monophasic, diphasic and rarely by triphasic spikes of 0.5–1.5 msec. duration and voltages usually about 50–100 μ V. but reaching 500 μ V. in exceptional cases. Prostigmine increases fibrillation in completely denervated muscle, but it may abolish traces of fibrillation in a muscle being re-innervated by regeneration of an interrupted nerve supply.

7. Following re-innervation the separate fibre potentials composing a motor unit may appear poorly synchronized and spatially dispersed within the muscle causing a polyphasic action potential in which the individual units may be separated as much as 10 msec. or more, but maintaining a constant time relation with each other upon repeated firing of the same unit. These disintegrated units are thought to be due to abnormal ramification of the terminal axonal branches in the regenerated nerve terminals in addition to their abnormally slow velocity of conduction.

8. In muscles sensitized by denervation, mechanical stimulation by the needle tip serves to initiate not only a series of fibre potentials of the usual form, but also a series of repeated sharp waves usually of positive electrical sign at the needle tip. These appear to be non-propagated local potentials with form similar to a condenser discharge. They were not observed in normal muscle. These potentials are distinct from any other form of muscle action potential and they appear to be associated with local contractile processes induced by mechanical stimulation in a sensitized muscle.
(Authors' abstr.)

Action Potentials of Cerebellar Cortex in Response to Local Electrical Stimulation.

1. Electrical stimulation at or near the surface of a folium of the cerebellum results in the activation of elements thought to be the molecular fibers.

2. These conduct in a lateral direction at a rate of 0.35–0.50 meters per second and to a distance usually not exceeding 5 mm.

3. They, in turn, are capable of synaptically affecting the Purkinje cells.

4. Purkinje cells exhibit a negative potential in or near their dendritic processes whose duration is from 5 to 25 msec.

5. This potential may or may not be associated with an axon spike in the Purkinje cell fiber.

6. Evidence is obtained which leads to the belief that the synaptic delay for this Purkinje cell potential is of the order of 1 msec.
(Author's abstr.)

Selective Destruction of Large Motoneurons by Poliomyelitis Virus. (I) Conduction Velocity of Motor Nerve Fibers of Chronic Poliomyelitis Patients.

1. Maximal muscle action potentials evoked by appropriate motor nerve stimulation and conduction velocities of the fastest nerve fibers innervating these muscles have been studied in 26 human chronic poliomyelitis patients.

2. The conduction velocities of the fastest residual motor nerve fibers are slower than normal in this disease and vary directly with the action potential amplitude (i.e. functional ability) of the muscles they innervate.

3. Explanations for the slower than normal conduction rates are considered. The most likely cause is thought to be the selective destruction by the virus of those motoneurons with the thickest axons.

4. The mechanism of this proposed preferential invasion and killing by the virus—e.g. metabolic, mechanical, etc.—requires further study.

5. The results are discussed in the light of some of the pathological physiology of the disease.
(Author's abstr.)

Synaptic Facilitation in the Crayfish.

The same efferent fibers in the third root of the abdominal ganglia of the crayfish, *Cambarus clarkii*, can be activated by four independent preganglionic pathways.

These are the homolateral lateral giant, the two medial giants and the homolateral first root of the same ganglion.

In preparations in which the third root no longer responds to a single impulse in any preganglionic fiber, two shocks with variable time intervals were given to various pairs of pathways. With most combinations it was found that no summation occurs when the shocks follow each other closely. The length of this "inert period" depends on the distance between the synapses, being longest between the synapses that are furthest apart.

It is concluded that the normal summation periods are caused by a process which spreads along the postganglionic fiber from the first synapse stimulated. This process increases the excitability of the fiber at the neighbouring synapses. It diminishes in intensity with distance as well as with time. Transmission is not possible at the second synapse activated until this process has reached it. With certain combinations, especially that of the two medials, summation does occur when the impulses arrive at the ganglion at the same time. This summation most likely involves the excitation of only one synapse, which is partially activated by the first pathway stimulated and is then fully activated by the action potential of the second giant stimulated. (Author's abstr.)

Excitability Cycle and Interaction in Geniculate-striate System of Cat.

- 1. The postsynaptic negative spike observed in the lateral geniculate exhibits the general properties of soma potentials.
- 2. The potential magnitude recorded from a group of units (geniculate or cortex) shows a summation or recruitment interval extending to 30 msec. and a subnormal phase lasting for seconds.
- 3. The relative recruitment is greater in the subnormal phase and proportional to it by a function not yet defined. It is partly proportional to subliminal fringe and hence an inverse function of strength of stimulus, or of excited zone dimensions.
- 4. The subnormal phase in the geniculate has never been observed to develop fast enough to quench the first three responses occurring within the initial period of about 5 msec. This initial extinction phenomenon is not necessarily part of the conventionally defined subnormality, however.
- 5. It is not certain that the first cortical spike is entirely due to radiation fiber action potential.
- 6. Bilateral interaction occurs at cortical level for all components, but comparable interaction has not been demonstrated anywhere in the geniculate. (Author's abstr.)

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- *Inheritance of EEG Pattern in Children with Behavior Disorders. *Kennard, M. A.* 151

Inheritance of Electroencephalogram Patterns in Children with Behavior Disorders.

1. In the families of children with behavior disorders there is a marked similarity in EEG pattern in the various members of a single family. This is very obvious in members of a family who are of similar age. It is present even in the EEG patterns of parents and their children. A similar familial patterning has been shown in the families of epileptics.

2. There is a higher incidence of dysrhythmic and hence abnormal records in the patients (60 per cent.), than in their "normal" relatives (40 per cent.).

3. The incidence of EEG's in the "normal" relatives having 40 per cent. abnormality is different from that of the total normal population, which has only 10-15 per cent. of abnormal records.

4. It is suggested that anxiety or tension may be related to dysrhythmic and unstable EEG patterns, and that, in consequence, a very high incidence of abnormal EEG's appears in the neurotic or psychotic members of families with relatively unstable psychological background. This is reflected more in the EEG's of children than of adults because the cortical potentials of the former are, under any circumstance, more labile than are those of the latter. (Author's abstr.)

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1. Psychiatry.

Frontal Lobe Ablation in Chimpanzee: A Résumé of "Becky" and "Lucy." *Crawford, M. P., Fulton, J. F., Jacobsen, C. F., and Wolfe, J. B.* [*The Frontal Lobes*, 3.]

The reactions of 2 adolescent chimpanzees in problem-solving situations (tool usage, problem-box, delayed reaction set-up) were studied prior to and after unilateral ablation and following bilateral lobectomy. Follow-up observations were

made at intervals for 3 years. Protocols are given and results at retest periods are presented in detail. In general, bilateral ablation, as opposed to unilateral, resulted in "profound behavioural deficit," but continued post-operative training was accompanied in some problems by improvement. Variability in performance remained "the most clearcut feature." Discussions by W. Freeman, C. F. Jacobsen. L. A. PENNINGTON (Psychol. Abstr.).

Specialization of Behavioral Functions and the Frontal Lobes. Halstead, Ward C. [The Frontal Lobes, 59.]

A summary of the author's monograph (1497) is given with special emphasis placed upon the 4-factor theory of biological intelligence, upon the measurement of these factors in relation to the calculation of an impairment index. The inferences are made that biological intelligence is cortically represented as a gradient maximal in the frontal lobes, and that the four factors in unified fashion shed light upon ego functions. L. A. PENNINGTON (Psychol. Abstr.).

Some Connections of the Frontal Lobe Established by Physiological Neuronography. McCulloch, Warren S. [The Frontal Lobes, 95.]

Ten figures are presented to illustrate in summary the neural relations between the two or more sectors of the frontal lobes and between these and thalamic nuclei as inferred from the electrical reactions to local strychninization (neuronography). Brodmann's numbers are used, although no histological differentials are implied. The mechanism by which frontal lobe suppressor areas (8, 48, 24) operate is considered. L. A. PENNINGTON (Psychol. Abstr.).

The Non-pyramidal Motor Projections from the Frontal Cerebral Cortex. Mettler, Fred A. [The Frontal Lobes, 162.]

By comparing the capacities of primates bilaterally devoid of frontal cortex with primates sustaining pyramidotomy the author reviews the recent experimental and selected clinical literature on (1) the non-pyramidal motor functions of the frontal cortex, and (2) the pathways, as far as these are known or suspected, originating in the cortex by means of which the non-pyramidal motor functions are mediated. Brodmann's area designations and their subcortical terminations are tentatively specified and charted. Stress is placed upon the specialists' need to consider both cortical pyramidal and non-pyramidal factors in cases of motor dysfunctions. L. A. PENNINGTON (Psychol. Abstr.).

The Thalamic Projection to the Frontal Lobe. Freeman, Walter, and Watts, James W. [The Frontal Lobes, 200.]

By recourse to methods of defibrillation dissection, myelinization and retrograde degeneration changes in the thalamus following frontal lobotomy in 14 cases, the cortico-thalamic relationship is described at the human level. It is concluded, to illustrate, that all parts of the frontal lobe receive projection fibers from the thalamus; that "there is no frontal association area"; that retrograde degeneration of the medial thalamic nucleus "may be an important factor" in relief from emotional tension after lobotomy. Projection of this nucleus upon the cortex is described and charted. L. A. PENNINGTON (Psychol. Abstr.).

The Motor Functions of the Agranular Frontal Cortex. Denny-Brown, D., and Botterell, E. H. [The Frontal Lobes, 235.]

Reports of clinical observations made upon the macaque monkey exposed to ablation studies (with appropriate histological and other controls) provide a "reappraisal of some of the facts of motor disorder from frontal lesions" with special reference to areas 4 and 6. Selected results show that "what is represented in area 4 is the whole motor mechanism, and especially the red nucleus, reticular formation and propriospinal internuncial neurons of the cord. The direction of patterns of behavior is determined elsewhere." Ablation of all of area 4 gives rise to spasticity. These and other findings are discussed clinically, theoretically, and in relation to Betz-cell distribution. Comments by J. F. Fulton, P. C. Bucy, F. A. Mettler. L. A. PENNINGTON (Psychol. Abstr.).

Movement of Head and Eyes from Stimulation of Human Frontal Cortex. Rasmussen, Theodore and Penfield, Wilder. [*The Frontal Lobes*, 346.]

In a series of 208 electrical stimulations made during craniotomies performed under local anesthesia, eyeball movement was elicited in 48 stimulations in 31 cases. A third of the points were anterior to the central sulcus; the remainder were located in the anterior half of the precentral gyrus or in the caudal segment of the adjacent frontal convolutions. Head movements, nonspecific in type, were aroused from stimulation of the precentral gyrus at the central sulcus. It is suggested that eye movement elicitation cannot be limited to any one fronto-cortical area inasmuch as areas 4, 6 and 8 are in different cases responsible.

L. A. PENNINGTON (Psychol. Abstr.).

Some Forebrain Mechanisms Involved in Expression of Rage, with Special Reference to Suppression of Angry Behavior. Bard, Philip, and Mountcastle, Vernon B. [*The Frontal Lobes*, 362.]

By means of surgical, observational and histological methods the effects of extirpation of neocortical tissue upon rage behaviour of 5 cats are studied. Results suggest that these animals become quite placid after removal of the neocortex, but that rage reactions are easily aroused following injury to the limbic lobe in these animals or in other subjects with intact neocortex. It is held that under normal circumstances the limbic lobe inhibits the rage mechanisms centered subcortically, and that the cells of the limbic lobe are in turn inhibited by the cells of the neocortex. These and other findings are related to current studies and theory wherein continued research is held necessary to clarify controversial points. Comments by P. C. Bucy, Margaret A. Kennard, R. M. Brickner.

L. A. PENNINGTON (Psychol. Abstr.).

Stimulation and Regional Ablation of Orbital Surface of Frontal Lobe. Livingston, Robert B., Fulton, John F., Delgado, Jose M. R., et al. [*The Frontal Lobes*, 405.]

One hundred controlled observations of preoperative and normal monkeys (15) and chimpanzees (2), the animals subjected to ablation of all or parts of the orbital surface (Walker's area 13), suggest that bilateral extirpation is accompanied by hyperactivity (8 to 16 times the normal), by heightened body-extremity temperature and by augmented reflex vasodilatation. After indicating the limitations of the electrical and ablative techniques the authors conclude by presenting detailed analysis that the orbital surface "is related both to autonomic and somatic mechanisms" perhaps by way of mesopallial connections with the cortex, thalamus, hypothalamus, and extrapyramidal systems, and that this area can be considered a part of the "highest representation of visceral functions."

L. A. PENNINGTON (Psychol. Abstr.).

The Anterior Cingulate Gyrus and Personality. Ward, Arthur A., jun. [*The Frontal Lobes*, 438.]

The neuroanatomy of the anterior limbic region (Brodmann's area 24) is described and the effects both of electrical stimulation and ablation in the monkey are reported. Evidence shows the region to have two powerful functions, viz., "suppression" of cortical activity and motor performance as well as "domination" of the autonomic nervous system. Absence of data at the human level precludes concise statements with reference to progressive personality changes, although the "mental" effects of tumors of the anterior corpus callosum might perhaps be due to limbic-lobe involvement.

L. A. PENNINGTON (Psychol. Abstr.).

Effect of Extirpation of Frontal Areas upon Learning Performance of Monkeys. Harlow, Harry F., and Settlage, Paul H. [*The Frontal Lobes*, 446.]

The effects of unilateral and bilateral cortical lesions (especially frontal in locus) on the learning behaviour of 8 monkeys and their controls in 5 test situations are summarized. Results indicate a quantitative and significant inferiority for the operated animals on all tests, with greatest deficit on reversal problems. Whether this partial loss is "general" or a function of "special abilities" is as yet unknown. It is concluded that the results predicate similar deficits in man following frontal lobectomies and lobotomies.

L. A. PENNINGTON (Psychol. Abstr.).

Normal and Pathological After-discharge from Frontal Cortex. Walker, A. Earl, and Johnson, Herbert C. [The Frontal Lobes, 460.]

The electroencephalographic recordings (8-channel machine) of waves immediately following experimental electrical stimulations of the frontal lobes in 6 normal monkeys, in 20 animals prepared by earlier placement of alum protein plaques on the frontal cortex; in 10 monkeys each with a coil beneath the scalp with terminals in the cortex, provide data that characterize "normal" and "abnormal" self-sustained responses. Selected results indicate the frontal cortex to have the highest threshold, the motor the lowest threshold, the longest acting and most radiating after-discharge. The waves of the "plaque" subject, however, showed a low threshold, wide areal involvement, marked variability in cessation (some stop, start up again and continue for 2 or more hours). Physiologically this datum appears "to play a large role in epileptic activity."

L. A. PENNINGTON (Psychol. Abstr.).

Report of Case of Bilateral Frontal Lobe Defect. Ackerly, S. S., and Bentor, A. L. [The Frontal Lobes, 479.]

The neurological, familial, psychological, nosological and etiological aspects, based upon repeated studies during the last 21 years of a 35-year-old white male suffering from bilateral frontal lobe defect, are discussed. Although most psychometric findings (Rorschach and Kohs Blocks, for example) were negative, the patient whose social behavior superficially suggested that the psychopathic personality was unable socially to plan, to pursue a remote goal. He lacked the "abstract attitude" described by Goldstein, was free from anxiety. The chapter supplies the literature with "confirmatory evidence that the frontal lobes are essential . . . for the amplification and elaboration of experience."

L. A. PENNINGTON (Psychol. Abstr.).

The Frontal Homolateral Syndrome in the Light of Observations made on 150 Cases of Traumatic Lesions. Rouquier, A. [The Frontal Lobes, 505.]

The author describes the subjective and objective "elements" that comprise the recently identified aforementioned syndrome, and relates these to neurological involvements in areas 9, 10, 11, 6 α , β . The outward deviation of the outstretched arms (eyes closed), the lowering and falling of the corresponding limbs, homolateral trembling and the dysmyotonic reaction, as syndrome "signs," are described and clinical tests for each indicated. "The frontal convolutions . . . play a very important role in reactions of the head and trunk as well as in the limbs," and they are important "sympathetic and intellectual centers." The neural mechanisms mediating these signs are conjectured.

L. A. PENNINGTON (Psychol. Abstr.).

Symposium on Gyrectomy. Penfield, Wilder, Cameron, D. Ewen, et al. [The Frontal Lobes, 519.]

As a substitute for leucotomy procedures 7 patients exhibiting prolonged tension and anxiety were treated by bilateral symmetrical removal of frontal cortex in areas connected with the thalamus, and post-operatively compared with 8 patients of similar diagnosis treated by bilateral frontal lobotomy. Administration of a wide range of psychological and stress tests shows post-operatively a "consistent slight drop in general intelligence, a significant reduction in vocabulary" (in the direction of concreteness). These and other differences are considered as conceivably due to the patients' inability to maintain a "set in the face of interference." The chapter is divided into 3 parts. The first by Penfield discusses operative techniques and anatomy. The second, by D. E. Cameron and M. D. Prados, provides a summary of psychiatric findings, among which is the statement, "gyrectomy is of no greater value than lobotomy." The third, by R. B. Malmo, describes in detail the psychological approach to the problem.

L. A. PENNINGTON (Psychol. Abstr.).

Motor Aphasia and Agraphia Caused by a Small Vascular Lesion Confined to Third and Second Convolutions of Left Frontal Lobe. Scheinker, I. M., and Kuhr, B. M. [The Frontal Lobes, 582.]

A clinical description of the aphasic and agraphic behavior of a 61-year-old male is given. Upon his decease, macroscopic and microscopic studies were made

of the brain, revealing a "sharply demarcated area of hemorrhagic softening confined to the upper half of the third and lower third of the second frontal convolution on the left." These observations are related briefly to the historical findings by Broca, Marie and others. L. A. PENNINGTON (Psychol. Abstr.).

The Cortical Motor Pattern Apraxias. Nielsen, J. M. [*The Frontal Lobes*, 565.]

The 3 types (ideational, ideokinetic, cortical motor pattern) of apraxia are defined and described, the experimental and clinical approaches to the subject historically summarized. Major attention is given the latter type of apraxia wherein 3 subtypes are identified, their cortical centers specified on the grounds of clinico-pathological findings. Three illustrative case-histories are given.

L. A. PENNINGTON (Psychol. Abstr.).

Effect of Cortical Excision and Stimulation of the Frontal Lobe on Speech, with a Review of Aphasia and Cerebral Physiology Related to Speech. Robb, J. Preston. [*The Frontal Lobes*, 587.]

Following a review of the recent experimental and clinical literature summarizing the results accruing from cortical stimulation and ablation methods in relation to the anatomical basis of speech, the author sequentially reports observations made on 27 cases of right-handed patients who were treated (1930-1947) for focal epilepsy by surgical excisions from the left frontal lobes. Results include (1) no residual speech defect in 26 cases; (2) the left hemisphere was found dominant in 16 cases; (3) all of the lateral aspect of the lobe with the exception of the posterior part of the 3rd convolution can be ablated with, at worst, only transient aphasia; (4) speech recovery does occur after excision of the posterior part of the 3rd convolution. The value of electrical stimulation (Rahm stimulator) as an adjunct to surgery and research is stressed. Results are discussed briefly in relation to the problem of bilateral localization of speech functions.

L. A. PENNINGTON (Psychol. Abstr.).

Autonomic Functions of Frontal Lobes: Studies on Patients with Head Trauma. Netsky, Martin G., and Starr, Harry. [*The Frontal Lobes*, 610.]

Fifty servicemen, 19 to 38 years of age, and all having a year earlier sustained head injuries, and now all undergoing treatment for consequent post-traumatic seizures, were studied before and after craniotomies (performed by A. Earl Walker) with reference to selected autonomic functions, including sweating, skin temperature, blood pressure. Observations of control and experimental subjects indicate that autonomic changes, especially those of sweating and skin temperature, "were related to a contralateral area of the cortex, extending anteriorly from the post-central gyrus to an undetermined distance beyond the precentral gyrus . . . the representation of autonomic influence in the cortex was analogous in position to the somatic." These and other findings are related to recent research studies on cortico-autonomic correlations.

L. A. PENNINGTON (Psychol. Abstr.).

Psychological Changes Produced by Frontal Lobotomy. Yacorzynski, G. K., Boshes, Benjamin, and Davis, Loyal. [*The Frontal Lobes*, 642.]

Detailed and repeated psychological examinations (21 different tests) of a 36-year-old male patient in good contact were made prior to and after lobotomy. Results include: (1) the observation that the operation was accompanied by none of the changes consequent to frontal lesions; (2) no evidence for a change in motivation (aspiration level and degree of effort tests); (3) a decrease of 17-18 I.Q. points on the Wechsler Scale with greater loss on the verbal scale—especially on arithmetic reasoning; (4) lowered performance on the Vigotsky test and in those reasoning test situations demanding the "use of concepts removed from immediate experience"; (5) while the Rorschach suggested the release of a psychosis, clinical impression and the MMPI psychogram suggested improvement. These and other test results are "speculated" upon in relation to theory and to the variant results that obtain from lobectomies.

L. A. PENNINGTON (Psychol. Abstr.).

Telencephalization of Survival Characteristics. Brickner, Richard M. [*The Frontal Lobes*, 658.]

The absence of "neurological comprehension" of the manner by which the nervous system participates in the mediation of prehuman attributes leads the

author to propose and develop the thesis that the cortex "instead of being principally devoted to the *suppressing* of what we call primitive impulses, actually has as one of its chief functions the *expressing* of these impulses" (survival functions). "This results from . . . the familiar process of encephalization." These survival characteristics (rage, for example) are telencephalized by all persons, the form determined by the culture. Thus, telencephalization is the neural process underlying acculturation, wherein culture promotes repressions of certain ways of expressing the survival functions. It is then posited that most social and personal problems arise from normal rather than from abnormal behavior and that much needed social therapy must be telencephalized through insight.

L. A. PENNINGTON (Psychol. Abstr.).

Personality Analysis Before and After Frontal Lobotomy. Rylander, Gosta. [*The Frontal Lobes*, 691.]

An analysis of the "changes in detail" that accompany leucotomy is made by careful observational and psychometric pre-operative and post-operative study of 8 of a series of 32 patients in the group reported upon. Descriptions of interest loss, of "shallowness and forgetfulness" are given, as well as a characterization of the patients' "reduction" in attention, in word-naming, and in I.Q. scores (Stanford Revision). These and other findings lead to a conclusion of reluctance to use this surgical method upon nonpsychotic patients . . . and these "findings are at least a warning that intellectual damage may follow lobotomy." Discussion by R. M. Brickner, W. Freeman, D. M. Rioch, R. R. Grinker, J. M. Nielsen.

L. A. PENNINGTON (Psychol. Abstr.).

Relief of Intractable Pain of Organic Origin by Frontal Lobotomy. Falconer, M. A. [*The Frontal Lobes*, 706.]

Medical and psychometric descriptions are given of one case of post-herpetic neuralgia and of one of tabes dorsalis both successfully treated by lobotomy. The finding earlier reported by Freeman and Watts, that the chief effect of the operation is to modify the patient's reaction to pain rather than to abolish pain perception is reiterated. This surgical approach is suggested as a last resort in such cases because of the personality changes observed to accompany the operation.

L. A. PENNINGTON (Psychol. Abstr.).

Frontal Lobotomy in the Treatment of Unbearable Pain. Watts, J. W., and Freeman W. [*The Frontal Lobes*, 715.]

The positive ("striking") effects of lobotomy upon a series of organic cases where unbearable pain, continuous or paroxysmal, was a major complaint are reported by describing the pre- and post-operative reactions of 9 patients (carcinoma, thalamic syndrome, tabes dorsalis, causalgia, phantom limb, atypical facial neuralgia). It is posited that the operation "interrupts the central process" responsible for reaction to pain as a threat. "Pain then becomes a sensation only."

L. A. PENNINGTON (Psychol. Abstr.).

The Psychological Effects of Frontal Lobotomy Performed for the Alleviation of Pain. Koskoff, Y. D., Dennis, Wayne, et al. [*The Frontal Lobes*, 723.]

The effect of lobotomy in the relief of chronic pain is studied, with appropriate controls, by reference to 10 patients (several "somatic," others "psychic") whose symptoms are reported (1) medically and clinically, (2) psychometrically (7 cases). In the latter, the Wechsler, Babcock-Levy, Porteus Maze, Rorschach, TAT and Goodenough Drawing tests are administered to the "organic" patients before operation and again 3 months afterward. All organic-pain cases free from "mental abnormality" showed some loss in intellectual abilities of a general type followed by, it is believed, a gradual restitution. The danger of generalizing from so few cases is stressed, present results being reported as "trends." Data obtained from the administration of personality tests are to be reported later.

L. A. PENNINGTON (Psychol. Abstr.).

Measurements of Heat Stimulus Producing Motor Withdrawal Reaction in Patients following Frontal Lobotomy. Chapman, William P., Rose, Augustus S., and Solomon, Harry C. [*The Frontal Lobes*, 754.]

The pre- and post-operative reactions of 23 patients (19 schizophrenics, 1 involutional melancholia, 3 psychoneurotics) to heat stimuli are studied in order to measure experimentally one aspect of the clinical observation that such patients show "an increased withdrawal reaction . . . to discomforting stimuli." For this the Hardy-Wolff-Goodell pain threshold apparatus was used; the heat required on the forehead to induce a wince and a head withdrawal was recorded. Post-operative retests were continued at intervals for 12 months. Wince and pull-away responses were significantly more easily elicited (lower threshold) after operation with this difference still present (although less so) 12 months later. "We have no explanation for the apparent discrepancy between these results and the fact that frontal lobotomy relieves intractable pain."

L. A. PENNINGTON (Psychol. Abstr.).

A Co-operative Clinical Study of Lobotomy. Moore, B. E., et al. [*The Frontal Lobes*, 769.]

As a co-operative inter-agency research program initiated in 1946, 200 chronic institutionalized cases (163 schizophrenics, 10 manic-depressives, 8 involuntions, 4 psychoneurotics, 15 miscellaneous) were studied, pre- and post-operatively, according to uniform procedures previously agreed upon. Follow-up studies at 1, 3, 6 and 12 post-operative months were made. Selected results include, (1) the patient's condition by 3 post-operative months is a "good indication" of future developments in his case; those showing moderate to marked improvement continue to improve; (2) paranoid schizophrenics show the best prognosis, with catatonics second; (3) improvement among schizophrenics is unrelated to the length of hospitalization, but this is less true among non-schizophrenic patients; (4) 75 per cent. of the 200 patients showed an amelioration of those symptoms most troublesome to personnel (suicide attempts, etc.); (5) sex and intelligence can be ignored as prognostic criteria. L. A. PENNINGTON (Psychol. Abstr.).

2. Biochemistry, Physiology, Pathology, etc.

Determination of Proteins in Cerebro-spinal Fluid. R. G. Willcocks. [*Nature*, **163**, 329-30 (1949).]

A rapid, approximate method for medical use has been devised. The xanthoproteic reaction was made quantitative and compared with an artificial standard; $\text{mg. per cent. protein} = T/S \times c \times 1.6$, where T/S = ratio of color intensities of sample and standard and c = concentration of the standard $K_2Cr_2O_7$ in mg. per cent. A hollow wedge colorimeter was used. No data on tests of the method are included. E. NEWTON (Chem. Abstr.).

Chemical Analysis of Spectrophotometric Findings in the Cerebrospinal Fluid. Spiegel-Adolf, M., Wycis, H. T., and Spiegel, E. A. [*Science*, **109**, 335-6 (1949) cf. C. A., **42**, 3480c.]

Cerebrospinal fluids from 40 patients with organic or functional nervous disorders were examined for ultra-violet absorption at 2650 Å, ascorbic acid content, total protein, globulin, cell count, and Wassermann, and colloidal gold tests. Ascorbic acid values were converted into extinction coefficient (E) and subtracted from experimentally determined E of the cerebrospinal fluid, resulting in a difference D_1 . Protein values were likewise converted, a residual value D_2 being obtained. Three groupings of D_1 , 0-0.4, 0.41-0.8, 0.8-2.5, and D_2 , 0.0-14, 0.14-0.61, 0.61-2.16 were made, the values varying in different types of disorders. Selective cerebrospinal fluid absorption is not always explained by ascorbic acid and protein content. D_2 values were particularly pronounced in central nervous system tumors, where destruction of nuclear substances may be expected. The differences between the mean E of normal cerebrospinal fluid, and that of fluid withdrawn 1 hour to 2 months after cerebral concussion were statistically significant, and D_2 values above normal were noted in the fluid shortly after such concussion. The D_2 values

are believed due primarily to nuclear substance constituents, such as purine-pyrimidine compounds, which may be nucleic acids or their cleavage products.

JOHN P. CRISPELL (Chem. Abstr.).

Thiaminase and the Action of Acetylcholine on the Heart. Bettencourt, J. Moniz de, and Abecasis, L. [Compt. rend. soc. Biol., **142**, 1147-8 (1948).]

In the perfused turtle heart, added thiaminase destroys thiamine and thereby makes the heart less sensitive to acetylcholine. L. E. GILSON (Chem. Abstr.).

Behaviour of Ocular Tension and Retinal Arterial Pressure in Acetylcholine Shock. Rosso, Silvio. [Rass. ital. Ottalmol., **16**, 357-69 (1947).]

In 15 young schizophrenic patients undergoing shock therapy by rapid intravenous injection of 0.5 gm. acetylcholine bromide in 2 ml. water, during 90 seconds after injection the systolic blood pressure usually fell 20 mm. Hg, the retinal arterial pressure decreased 5-15 mm., and the intraocular pressure was lowered 5 mm. Hg (average). The retinal arteries appeared to become first constricted and then dilated.

W. M. GRANT (Chem. Abstr.).

Convulsant Action of Acetylcholine. Arduini, A., and Machne, X. [Arch. fisiol., **48**, 152-67 (1949).]

In unanesthetized rabbits Jacksonian epilepsy was caused by acetylcholine 4-10 per cent. applied to the masticatory cortex. The effect was increased by 1 per cent. eserine, and prevented by intravenous atropine 1 mgm./kgm. No similar effect was seen after application of saline of equal tonicity.

H. L. WILLIAMS (Chem. Abstr.).

The Mechanism of Action of Barium Chloride and Acetylcholine in Biological Systems. Capraro, V., and Barilli, V. [Arch. intern. Physiol., **56**, 241-4 (1949).]

The following observations demonstrate that BaCl_2 does not act entirely through the liberation of acetylcholine (1) : (1) BaCl_2 suppresses the action of (1) in the isolated frog or rabbit heart. (2) In the isolated frog heart, atropine inhibits the action of (1), but not that of BaCl_2 . (3) KCl diminishes the contraction of the isolated small intestine of the guinea-pig produced by BaCl_2 , but not that caused by (1).

FRED H. SNYDER (Chem. Abstr.).

Cholinesterase in Blood and Spinal Fluid in Psychiatric Cases. Glasson, B., and Nutrix, S. [Presse Méd., **55**, 230-1 (1947).]

See C. A., **42**, 3480d.

A. E. MEYER (Chem. Abstr.).

Thiamine and the Inhibition of Cholinesterase by Eserine. Bettencourt, J. Moniz de, and Cardoso, M. Rodrigues. [Compt. rend. soc. Biol., **142**, 1149 (1948).]

In guinea-pig serum *in vitro* the activity of cholinesterase inhibited by eserine is not restored by addition of thiamine.

L. E. GILSON (Chem. Abstr.).

Correlation between Signs of Toxicity and Cholinesterase Level of Brain and Blood during Recovery from Diisopropyl Fluorophosphate (DFP) Poisoning. Freedman, A. M., Willis, Alice, and Himwich, H. E. [Am. J. Physiol., **157**, 80-7 (1949); cf. C. A., **42**, 7450a.].

After the injection of large doses of DFP non-specific plasma cholinesterase regenerates more rapidly than the specific cholinesterases of the red blood corpuscles and the brain. A lag in regeneration of erythrocyte cholinesterase activity lasting from 24 to 48 hours occurs after injection of DFP, a period during which brain cholinesterase regenerates rapidly. Subsequently the rate of regeneration of erythrocyte cholinesterase becomes more rapid and surpasses that of the brain. A close relation appears to exist between the severity of the toxic signs of DFP poisoning and the level of brain cholinesterase during the regeneration period. The relation between toxic signs and erythrocyte cholinesterase activity is less exact, and fails altogether in the case of the plasma.

E. D. WALTER (Chem. Abstr.).

Relation between Cholinesterase Inhibition and Function in a Neuroeffector System. Riker, Walter F., jun., and Wescoe, W. Clarke. [*J. Pharmacol. Exptl. Therap.*, **95**, 515-27 (1949).]

The rate of irreversible inactivation of cholinesterase (I) in the submaxillary gland of the cat by diisopropyl fluophosphate (DFP) shows the characteristics of a first order reaction. Approximately 50 per cent. of the glandular (I) can be inhibited without affecting response to electric stimulation of the chorda tympani. Beyond this point changes in function accompany further progressive inactivation of (I). These changes include a decrease in the frequency of stimulation required to elicit a threshold response, a prolongation of the response to maximum stimuli, and eventually the onset of spontaneous salivary secretion when the (I) activity is reduced to 10 per cent. or less of the normal. These findings are discussed with respect to physiological and pharmacological interrelationships affecting chemical mediation at neuroeffector junctions.

L. E. GILSON (Chem. Abstr.).

Tubocurarine Antagonism and Inhibition of Cholinesterases. Blaschko, H., Bulbring, E., and Chou, T. C. [*Brit. J. Pharmacol.*, **4**, 29-32 (1949).]

The antitubocurarine (I) activity of a series of compounds related to prostigmine (II) was compared with their inhibitory action on true cholinesterase (III) of dog caudate nucleus and on the pseudocholinesterase of horse serum. There is a significant correlation between (I) activity and inhibitory action on true (III). This supports the view that it is the true (III) which is responsible for the destruction of acetylcholine at the site of its physiological action. Substitution of the Me groups on the quaternary N of (II) by Et at first increases both the (I) and the anti-(III) activity, but the peak is reached at the diethyl compound, and the activity of the triethyl compound is again much less. A strongly basic N radical in the phenolic moiety of the (II) molecule is indispensable not only for strong (I) activity, but also for a strong anti-(III) activity.

H. O. SINGHER (Chem. Abstr.).

Rate of Penetration of Electrolytes into Nerve Fibers. Rothenberg, Mortimer A., and Feld, Emily A. [*J. Biol. Chem.*, **172**, 345-6 (1948).]

The permeability of surface membranes to K, Na and Ca and their rate of penetration have been investigated with giant nerve fibers of squid exposed to artificial sea water in which normally occurring ions were replaced individually by radio-active K^{42} , Na^{24} or Ca^{45} , in equimolar concentrations. Concentration of each ion in the axoplasm increased, K^+ , which showed high concentration in axoplasm, penetrating within 60 minutes to a concentration double that outside the cell; Na^+ (low in axoplasm) penetrated rapidly for 15-20 minutes, then decreased, the amount inside the cell rising to 25-30 per cent. that outside; Ca^{++} (low in axoplasm) penetrated to a concentration 60-80 per cent. that outside. The ratio of the concentration of the 3 ions (C_i) compared to that outside (C_o) is a function of time of exposure. Results confirm that permeability requires an active process in surface membranes.

JOHN P. CRISPELL (Chem. Abstr.).

Carbonic Anhydrase in the Central Nervous System of the Developing Fetus. Ashby, Winifred, and Butler, Ellen. [*J. Biol. Chem.*, **175**, 425-32 (1948); cf. *C. A.*, **42**, 5105h.]

The central nervous system of the normal fetus of cattle exhibited a progressive rostral increase in carbonic anhydrase (I). (I) was absent from the cerebrum until shortly before birth; at birth the adult pattern of (I) was established. A similar increase of (I) occurred in the human fetus except that no (I) was found in the pallium of the full term infant. This finding is discussed.

JOHN HEARON (Chem. Abstr.).

Requirement for Diphosphopyridine Nucleotide in the Aerobic Metabolism of Pyruvate by Brain Tissue. Lerner, Joseph, Jandorf, Bernard J., and Summerson, Wm. H. [*J. Biol. Chem.*, **178**, 373-82 (1949).]

Diphosphopyridine nucleotide (DPN) was demonstrated to be an essential co-factor in the oxidation of pyruvic acid by H_2O -homogenized mouse brain. Other co-factors were inorganic $PO_4^{---}Mg^{++}$, adenosine triphosphate, fumarate,

and cytochrome c. The DPN requirement became apparent only after thorough homogenization of the tissue. When it was homogenized in 1-3 per cent. nicotinamide solutions instead of H_2O , it was unnecessary to add DPN. Since highly homogenized brain preparations had a higher DPNase activity than coarse homogenates, it is likely that intracellular DPNase is released or activated by thorough disintegration, thus promoting the decomposition of DPN present in the tissue. Nicotinamide apparently inhibited the DPNase activity.

ERICH HEFTMANN (Chem. Abstr.).

Presence of Histamine in Central Nervous System Extracts. Cicardo, V. H., and Stoppani, A. O. M. [*Nature*, **163**, 365 (1949).]

Histamine is the main agent responsible for the depressor effect produced when alcohol or aqueous extracts of ox- sheep, dog or rabbit brain are injected into laboratory animals. In dogs benadryl reduced the depressor effect induced by the extracts and small doses of histamine to the same degree. Atropine did not show this phenomenon. This histamine equivalent of the extracts was determined by comparison of the effect on arterial blood pressure of varying concentrations of extract with varying concentrations of histamine solutions. Acetone and CCl_4 COOH extracts gave similar results. Et_2O extracts were inactive. Further fractionation was carried out after purification of the extracts with basic lead acetate. The active portion was precipitated with phosphotungstic acid or Ag-Ba hydroxide, and the depressor effect of this portion was also inhibited by benadryl.

J. P. DANEHY (Chem. Abstr.).

Chemical Topography of the Trace Elements in the Brain of Man, according to Spectroscopic Analysis. Voinar, A. O., and Rusanov, A. K. [*Biokhimiya*, **14**, 102-6 (1949).]

The amount and distribution in the brain of the following trace elements (elements which form less than 1 per cent. of the ash) have been determined by their emission spectra: Ag, Al, Bi, Cr, Cu, Mn, Mo, Ni, Pb, Si, Sn, Ti, V, and Zn. Sections of the brain which differ in morphological structure and physiological function possess a different chemical composition of the trace elements.

H. PRIESTLEY (Chem. Abstr.).

Anaerobic Leakage of Potassium from Brain. Dixon, K. C. [*Biochem. J.*, **44**, 187-90 (1949).]

Considerable amounts of K leak into the extracellular fluid from the brain cells when their supply of O_2 and glucose is cut off. Since enzymic activity in the cells depends upon the high concentration of K, its loss may be responsible for the damage. The effect of the glucose is probably associated with its use in glycolysis. At any rate, inhibition of glycolysis by NaF causes a similar leakage of K from the brain cells, as it also does in the red blood cells.

S. MORGULIS (Chem. Abstr.).

Cytochrome c in Human Brain. Buscaino, Giuseppe Andrea. [*Acta Neurol. (Naples)*, **3**, 584-96 (1949).]

By the Fujita method cytochrome c was determined in 41 human brains; it was maximum (up to 22.85 mgm. per cent.) in the cerebral cortex, followed by the 3rd frontal, the striatum, thalamus, substantia nigra, postrolandic, calcarine, etc. Old subjects showed rather increased values. Brain patients showed in the various zones a lower concentration than normal subjects. In some specific diseases, as progressive paralysis, schizophrenia, and parkinsonism, the lower concentration of cytochrome c was found only in certain zones of the brain.

C. SCANDURA (Chem. Abstr.).

Biochemical Changes in the Blood Caused by Emotions. Cotugno, Vito. [*Arch sci. Med.*, **87**, 201-6 (1949).]

Emotions cause modifications in the glucose tolerance and in K and polypeptides in the blood. The modifications are related to the orientation of the autonomic system of the person.

A. E. MEYER (Chem. Abstr.).

Cerebral Constituents in Relation to Blood Gases. Gurdjian, E. S., Webster, J. E., Stone, W. E., and Kopala, J. [*Am. J. Physiol.*, **156**, 149-57 (1949); cf. *C. A.*, **43**, 3088c.]

Cerebral tissue from morphinized dogs was obtained for chemical analysis by freezing *in situ* with liquid air. Lactic acid, glucose, glycogen and acid-soluble P compounds were determined. Blood samples obtained immediately prior to the freezing were analysed for lactic acid, glucose, O, CO₂ and pH, and the tensions of O and of CO₂ were calculated. The effects of variations in the respired gas mixtures were investigated. Variation of arterial CO₂ tension in the presence of adequate O caused no significant changes in the cerebral constituents studied. Hypoxia induced an increase of lactic acid and a breakdown of phosphocreatine in the brain. These changes were diminished when the associated acapnia was counteracted by adding CO₂ to the respired gas mixture. The cerebral adenosine triphosphate remained undecomposed during hypoxia until the extreme limit of tolerance was reached. At this point the phosphocreatine was almost completely decomposed and decomposition of adenosine triphosphate began. The cerebral glucose remained in the normal range during hypoxia. The glycogen values were normal. Changes of CO₂ tension did not play a major role in the regulation of the electro-corticogram either in the presence or in the absence of adequate O.

E. D. WALTER (Chem. Abstr.).

Influence of Atomic Decomposition Products on the Functional Condition of the Nervous System. Vasil'ev, L. L. [*Nauch. Byull. Leningrad. Gosudarst. Univ.*, No. **18**, 16-18 (1947).]

Alpha-particles (from polonium source) impacting on the sciatic nerve preparation (frog specimen) at 3-4 mm. distance, with stimulation of the nerve being produced by an induction coil (100 cycles per sec.), show an initial drop of stimulation threshold, followed by a rise to a steady level which maintains itself for 1-2 hours, after which a rapid decline sets in and the tetanic effects decline rapidly; the initial contractions become more prominent, followed by rapidly developing parabisis. The action of the exposure to alpha radiation is similar to the action of ultraviolet irradiation, and is complementary to the action of other parabiotic agents; thus 0.5 hour exposure followed by immersion in isotonic KCl produces parabisis in 9-10 minutes (instead of normal 12-15 minutes).

G. M. KOSOLAPOFF (Chem. Abstr.).

Carotid Sinus Discharge and the Adrenals. Arterenol as a Chemical Mediator of Sympathetic Nerve Stimulation and Hormone of the Adrenal Medulla. Holz, Peter, and Schumann, Hans Joachim. [*Arch. exp'tl. Path. Pharmacol.*, **206**, 49-64 (1949).]

In cats and dogs clamping both carotids provokes carotid sinus discharge, resulting in rise of blood pressure and contraction of the spleen, but no change in blood sugar and no inhibition of intestinal contractions. These effects are not those of adrenaline, but are like those of noradrenaline which presumably originates in the adrenal medulla.

L. E. GILSON (Chem. Abstr.).

Microchemical Studies of the Nervous System. VI. Water and the Sulphur-, Phosphorus-, and Nitrogen-containing Fractions of the Brain of the Newborn and Adult Mouse. May, Raoul Michel. [*Rev. can. biol.*, **7**, 642-61 (1948); cf. *C. A.*, **43**, 4308c.]

The methods of chemical analysis previously applied to degenerating brains and nerves (*C. A.*, **25**, 1562; **35**, 3301⁹; **42**, 5486d) were applied to the study of the brain cells of newborn, 7-day, 14-day, and adult albino mice. There was a decrease in water content from 86.93 in the newborn to 77.41 per cent. in the adult. On the dry basis total S decreased from 1.043 at birth to 0.719 per cent. in the adult; lipid S decreased from 0.183 to 0.116, with a temporary increase to 0.233 per cent. at 7 days; protein S increased from 0.300 to 0.371 per cent. On the dry basis total P increased from 1.892 at birth to 1.949 at 7 days, and dropped to 1.396 per cent. in the adult; lipid P increased from 0.549 at birth to 0.799 per cent in the adult; protein P decreased from 0.378 to 0.184 per cent. Total N decreased from 11.32 at birth to 9.67 per cent. in the adult; protein N, from 8.89 to 7.39 per cent.; lipid N increased during the first 2 weeks from 0.76 to 1.26, and fell to

0.70 per cent. in the adult. There is an increase in phosphatides during the post-natal myelinization. In all cases there was a decrease in water-soluble fractions during growth, in water-soluble S from 0.641 to 0.210, in water-soluble P from 0.895 to 0.357, in water-soluble N from 2.13 to 1.24 per cent. The results are also given as percentage of the fresh brain and as absolute weight during the growth of the brain. These figures, compared with those obtained in the study of nerve degeneration, show that in the latter process there is a differentiation of certain cellular constituents, and in addition there are special chemical transformations that are different from a simple reversion to the embryonic state. Quantitative analyses of the constituents of the nerve cells reveal variations which shed more light on their age, and consequently on their adaptive possibilities at a given stage of their growth, than the modifications revealed by presently known cytological techniques.

A. PAPINEAU-COUTURE (Chem. Abstr.).

Cell Reactions in the Hypothalamus following Overloading of the Antidiuretic Function. Hillarp, Nils Ake. [*Acta Endocrinol.*, **2**, 33-43 (1949).]

Cytological changes in the cells of the hypothalamus of rats have been studied during acute and chronic overloading of the antidiuretic function. Acute effects were obtained by intravenous or subcutaneous injections of 5 per cent. NaCl, and produced a distinct chromatolytic reaction in the nerve cells of the supraoptic nucleus and in the magnocellular portion of the paraventricular nucleus. Chronic effects were produced by giving NaCl in drinking-water as follows: 1.5 per cent. NaCl for one week, 2.0 per cent. and 2.5 per cent. for two weeks. Changes in the cells included cellular hypertrophy, an increase in the Nissl-substance, consisting of large coarsely granular aggregations in the periphery of the cell, and an increase in size of the nucleoli in both the supraoptic nucleus and the magnocellular portion of the paraventricular nucleus.

ELVA G. SHIPLEY (Chem. Abstr.).

The Localization of Hypothalamic Centers Controlling the Gonadotropic Function of the Hypophysis. Hillarp, Nils Ake. [*Acta Endocrinol.*, **2**, 11-23 (1949).]

Brain lesions of different sizes were made in various regions of the hypothalamus in female rats. From the results it appears the center for luteinizing hormone (LH) secretion is in the anterior hypothalamus, anterior and ventral to the paraventricular nucleus. Lesions in these areas produced follicles but no corpora lutea, and a condition of constant estrus. Lesions caudal to the paraventricular nucleus in the form of small bilateral basal injuries produce the same disturbance, indicating a fiber system originating in the anterior hypothalamus. Complete inhibition of LH does not seem to occur with destruction of the centre or the fiber tract.

ELVA G. SHIPLEY (Chem. Abstr.).

Psychotic States: Correlations of Biochemical and Histologic Changes in the Brain. Barondes, R. de Rohan, Kuhns, Ralph H., Levine, David I., and Strachan, C. E. [*Military Surgeon*, **104**, 278-85 (1949).]

A review attempting to correlate metabolic disturbances of glycogen, sulphhydryl, creatinine, lipides, glutamic acid, enzymes, etc., to psychotic and parapsychotic states.

B. LUSTIG (Chem. Abstr.).

Neuronal Changes Associated with Tetany of Alkalosis and Hypocalcemia. Koenig, Harold, and Koenig, Ruth. [*Proc. Physiol. Soc. Philadelphia*, Jan. 18, 1949; *Am. J. Med. Sci.*, **217**, 466 (1949).]

Hypocalcemic tetany decreased the cytoplasmic basophilia, and alkalotic tetany increased it in the large motor neurons of the spinal cord and brain-stem of cats.

MARION HORN PESKIN (Chem. Abstr.).

3. Pharmacology and Treatment.

Anticonvulsant Drugs: Mechanisms of Action and Methods of Assay. Goodman, L. S., Toman, J. E. P., and Swinyard, E. A. [*Arch. intern. Pharmacodynamie*, **78**, 144-62 (1949).]

The action of the anti-epileptic drugs is discussed with data on 4 methods of assay in rats.

M. L. C. BERNHEIM (Chem. Abstr.).

Vasomotor Drugs on the Convulsant Threshold in Rodents with and without Diphenylhydantoin. Hanzlik, P. J., Cutting, W. C., Hoskins, Dean, Hanzlik, Harold-Barnes, E. W., and Doherty, E. W. [*Stanford Med. Bull.*, **6**, 47-53 (1948).]

Ergotamine, ergonovine and fluid extract of ergot (I) consistently raised the threshold for electric convulsions in rabbits whether or not they had received intravenously 25 mgm. diphenylhydantoin (II)/kgm. body-weight 2 hours previously. (I) also had this effect on rats whether or not they had received 20-40 mgm. (II) gastrically 2-4 hours in advance. The actions of epinephrine, ephedrine, tyramine and amphetamine (III) on rabbits, and of (III) on rats were more variable, but these drugs usually raised the convulsive threshold moderately or negligibly in animals not treated with (II) and decreased the anticonvulsant activity of (II). NaNO_2 , papaverine, and aminophylline, especially the latter, reduced the thresholds in treated and untreated rabbits. The threshold in these animals was not appreciably affected by quinine, cinchophen, azosulfamide, parathyroid solution, or Ca gluconate.

MARSHALL E. DEUTSCH (Chem. Abstr.).

Effect of Convulsant and Anticonvulsant Agents on the Activity of Carbonic Anhydrase. Torda, Clara, and Wolff, Harold G. [*J. Pharmacol. Exptl. Therap.*, **95**, 444-7 (1949).]

Known methods for determining the activity of carbonic anhydrase from human blood *in vitro* are described. Low concentrations (0.0004 *M* or less) of convulsant drugs (acetylcholine, camphor, DDT, digitoxin, metrazole, picrotoxin, scilliroside, strychnine, ouabain) decreased the activity and anticonvulsants (hydantoin, methylphenylethylhydantoin, phenobarbital) increased it.

L. E. GILSON (Chem. Abstr.).

Antagonism between Metrazole and Anticonvulsants Demonstrated by the Rabbit Electroencephalogram. Bertrand, Ivan, Quivy, D., and Gayet-Hallion, Th. [*Compt. rend. soc. Biol.*, **142**, 1357-60 (1948).]

L. E. GILSON (Chem. Abstr.).

Anticonvulsive Action and Molecular Structure of Some Heterocyclic Pentagonal Compounds. V. Duration of the Anticonvulsive Action of Dimethyldithiohydantoin. Hazard, Rene, Cheymol, Jean, Chabrier, Pierre, and Smarzewska, Klaudia. [*Compt. rend.*, **228**, 958-60 (1949); cf. *C. A.*, **43**, 2324a.]

Intravenous injections of 25 mgm. pentetrazole per kgm. produce epilepsy-like crises, which, however, can be prevented by injections of 50 mgm./kgm. of Ca salt of dimethyldithiohydantoin (I). In experiment (a), a mixture of pentetrazole and (I) was injected intravenously into 4 rabbits. In (b) the pentetrazole injection was followed within 48 to 51 seconds by (I). In (c) (I) was injected first, followed by pentetrazole from 1 minute to 4 hours later. The best protection against convulsions was provided by (c) with an interval of 15 minutes between injections. This protective effect of (I) lasted several hours.

D. A. M. (Chem. Abstr.).

Curare-like Actions of Tri(diethylaminoethoxy) Benzene Triethyliodide. Mushin, Wm. W., Wien, R., Mason, D. F. J., and Langston, G. T. [*Lancet*, **256**, 726-8 (1949); cf. *W. Arch. intern. Pharmacodynamie*, **77**, 96 (1948); *J. Physiol. (London)*, **107**, 44 (1948).]

Flaxedil (I) in doses of 40-70 mgm. (about 1 mgm./kgm. of body-weight), injected intravenously in conscious persons, produced complete paralysis of the abdominal and forearm muscles without affecting the diaphragm or pulmonary ventilation. Recovery was full and complete within 30 minutes. The paralysis induced by (I) was rapidly neutralized by intravenous prostigmine.

BARBARA R. MURRAY (Chem. Abstr.).

Comparison of Decamethonium Iodide (C_{10}) with d-Tubocurarine in Controlling Electrically Induced Convulsions. Hobson, J. A., and Prescott, F. [*Lancet*, **256**, 819-20 (1949).]

C_{10} (I) (0.08 mgm./kgm. of body-weight) and thiopentone (bistrimethylammonium pentane diiodide) (C_5) were administered to 40 patients undergoing electroconvulsion therapy; at other times 20 of the patients received d-tubo-

curarine (0.3 mgm./kgm. of body-weight) (II). (I) was considered preferable to (II), since it did not produce histamine-like reactions, and the curarization produced by (I) passed off more rapidly. BARBARA R. MURRAY (Chem. Abstr.).

Curare and Curare-like Substances. Pharmacology and Clinical Use. Mussgnug, Gunther. [Pharmazie, 4, 17-20 (1949).] H. A. WEGNAR (Chem. Abstr.).

The Action of Synthetic Curarizing Compounds on Skeletal Muscle and Sympathetic Ganglia, both Normal and Denervated. Bulbring, Edith, and Depierre, France. [Brit. J. Pharmacol., 4, 22-8 (1949).]

The action of β -diethylaminoethoxy benzene ethiodide (I), 1, 3-bis (β -diethylaminoethoxy) benzene diethiodide (II), and 1, 2, 3-tris (β -diethylaminoethoxy) benzene triethiodide (III) was studied. On normal skeletal muscle (III) has a strong curarizing action against both electric stimulation of nerve to muscle and intra-arterial injections of acetylcholine (IV); (I) is one-fiftieth to one-twelfth as strong. This ratio of activity is reversed on the sympathetic ganglion whether it is stimulated through its preganglionic nerve or by intra-arterial injection of (IV), (I) being 50-100 times stronger than (III). On denervated skeletal muscle, stimulated by (IV), the ratio of activities of (I) and (III) is the reverse of that in normal muscle, provided that the doses of the curarizing agents are small. Large doses of (I) have a sensitizing action on denervated muscle; as the dose is increased the diminution of the muscle response to (IV) gives way to an augmentation. This effect has also been observed with *d*-tubocurarine (V). (I) and (V) both have a stimulant action by themselves on the normal as well as on the denervated sympathetic ganglion and on denervated muscle. A 50 per cent. inhibition of true cholinesterase (VI) of dog caudate nucleus was caused by (II) (10^{-3} M). (I) and (III) do not inhibit (VI) in this concentration. The muscle response to (IV) was depressed by (II) only in doses of about 1 mgm., and (II) was intermediate in potency between (I) and (III). H. O. SINGHER (Chem. Abstr.).

Effect of Extracellular Electrolyte Depletion on Brain Electrolyte Pattern and Electroshock Seizure Threshold. Swinyard, Ewart A. [Am. J. Physiol., 156, 163-9 (1949).]

Data are presented showing the distribution of water, Na, K, and Cl in the plasma and brains subjected to acute extracellular electrolyte depletion and subsequent replacement and the relation of these alterations to concomitant changes in electroshock threshold. The electroshock threshold is not closely correlated with total brain water or the calculated intracellular fluid volume; it is independent of the volume of extracellular fluid and of the intracellular K concentration. The electroshock seizure threshold is more closely correlated with extracellular Na and Cl concentration than with other factors examined.

E. D. WALTER (Chem. Abstr.).

The Action of Autonomic Drugs on Elasmobranch and Teleost Involuntary Muscle. Dreyer, N. B. [Arch. intern. Pharmacodynamie, 78, 63-6 (1949).]

Elasmobranch smooth muscle is not affected by pilocarpine. Acetylcholine causes contraction unaffected by atropine. Adrenaline, ergotamine and ergotamine are powerful stimulants, but ephedrine and amphetamine are without action. In teleosts, parasympathomimetic drugs are inhibited by atropine, and adrenaline causes relaxation.

M. L. C. BERNHEIM (Chem. Abstr.).

Central Inhibitory Effects of Carbon Dioxide. (II) *Macacus rhesus.* Stein, S. N., and Pollock, G. H. [Proc. Soc. Exptl. Biol. Med., 70, 290-1 (1949).]

Monkeys with screw-in electrodes fitted to the head were immobilized with dihydro- β -erythroidine and treated with various concentrations of CO_2 - O_2 mixture for different periods of time; then they were stimulated with threshold and super-threshold voltages. Concentrations of 20 per cent. or more of CO_2 prevented convulsions when inhaled for 3 minutes.

(III) *Man.* Pollock, G. H., Stein, S. N., and Gyarsfas, K. [Ibid., 291-2.]

CO_2 - O_2 mixtures were inhaled before a super-threshold shock current was applied for 0.5 seconds. With 30 per cent. CO_2 30 seconds of inhalation sufficed

to prevent convulsions; with 15-20 per cent. mixtures slightly longer period of inhalation were required.

(IV) *Convulsive Phenomena.* Gyarfás, K., Pollock, G. H., and Stein, S. N. [*Ibid.*, 292-3.] L. E. GILSON (Chem. Abstr.).

Central Impairment of Sympathetic Reflexes by 8-Aminoquinolines. Moe, Gordon K., Peralta, Braulio and Seevers, Maurice H. [*J. Pharmacol. Exptl. Therap.*, 95, 407-14 (1949).]

Pamaquine, pentaquine and isopentaquine chronically administered to dogs produce impairment of sympathetic cardiovascular reflexes, but not of parasympathetic or respiratory reflexes. The first 2 compounds cause similar effects in monkeys. It is believed that medullary cell groups are destroyed. 8-(2-(2-piperidyl)-isopropylamino)-6-methoxyquinoline (SN 13, 140) did not produce the above effects. L. E. GILSON (Chem. Abstr.).

Central Actions of Myanesin. Nicolau, Jose del Castillo. [*Arch. med. exptl. (Madrid)*, 11, 363-85 (1948).]

Experiments on decerebrate cats show a nonspecific inhibition of spinal reflexes by myanesin (I). Flexion and crossed extension are inhibited, the latter profoundly, but the knee-jerk is unaffected. The tonic cervical reflex induced by vertical flexion of the head is inhibited to the same degree as is crossed extension. Strychnine and (I) quantitatively antagonize one another, and eserine also antagonizes (I), especially with respect to crossed extension. The powerful inhibitory action of (I) on muscular tonus can be shown on normal, lightly anesthetized and decerebrate animals. (I) acts by specifically inhibiting internuncial neurons.

MARSHALL E. DEUTSCH (Chem. Abstr.).

Some of the Effects of Myanesin in Psychiatric Patients. Schlau, Louis S., and Unna, Klaus R. [*J. Am. Med. Assoc.*, 140, 672-3 (1949).]

Myanesin or tolserol (3-o-toloxyl-1, 2-propanediol) is a muscle-relaxing drug which does not affect voluntary muscle power, is not hypnotic, and does not affect responsiveness to external stimulation. It allays anxiety without clouding consciousness. S. MORGULIS (Chem. Abstr.).

Detoxication of Barbiturates of Short Action. Donatelli, L. [*Boll. soc. ital. biol. sper.*, 24, 461-2 (1948).]

After injection in rabbits, evipan, narconumal and eunarcon (methylated on N) were found most easily detoxicated, followed closely by pentothal; slower detoxication was noted for rectidon and pernocton (bromoallylated).

M. ELLIOTT (Chem. Abstr.).

Influence of Volatile Anesthetics and Barbiturates on Rate of Gastric Passage and Intestinal Absorption of Glucose Solutions in Rats. Cordier, D., and Chanel, J. [*Compt. rend. soc. biol.*, 142, 1120-2 (1948).]

Et_2O , CHCl_3 , phenobarbital and pentothal retarded passage through the stomach and absorption in the intestine. L. E. GILSON (Chem. Abstr.).

Some Pharmacological Properties of Sodium Ethyl 3, 3-Dimethylallylbarbiturate. Taylor, N. B. G., and Noble, R. L. [*Nature*, 163, 447 (1949).]

Sodium ethyl 3, 3-dimethylallylbarbiturate (I) produces stimulation of gastric and salivary secretion of central origin when administered to dogs and cats. (I) possesses an activity opposite to that of the ordinary hypnotic barbiturates. It produces an increase in blood pressure (even on intravenous administration), immediate marked stimulation of depth and frequency of respiration, and sharp increase in body temperature. Overdose in unanesthetized animals is associated with restlessness, muscular contractions, and violent convulsions leading to death, which may be due to respiratory muscle spasm. Sympathetic overactivity may occur. The LD_{50} (cats, rabbits) is 6.7 mgm./kgm., intraperitoneally or intravenously, with 3-4 mgm./kgm. producing symptoms. Under pentobarbital (II) anesthesia cats will tolerate 50 mgm./kgm. given over 4 hours, and 5 mgm./kgm.

produces a blood pressure rise which returns rapidly to normal. Isolated gut in Ringer's solution is stimulated, then narcotized, when concentrations of 0.01 per cent. (I) are reached. During the narcosis there is no response to added acetylcholine or histamine. The use of (I) as an antidote to overcome the undesirable effects of ordinary barbiturates is suggested. Preliminary work indicates that an anesthetic mixture of (I) and (II) may be given rapidly to rabbits by the intravenous route without producing respiratory paralysis.

JOHN P. CRISPELL (Chem. Abstr.).

A Study of Mescaline in Human Subjects. Salomon, Kurt, Gabrio, Beverly Wescott, and Thale, Thomas. [*J. Pharmacol. Exptl. Therap.*, **95**, 455-9 (1949).]

Five schizophrenic and one neurotic patient were given 200-400 mgm. mescaline sulfate (I) orally, and the urinary excretion of methoxyl groups was followed quantitatively for 18 hours (method described). (I) was identified in the urine, and most of the methoxy groups were probably present as (I). Methoxyl groups belonging to breakdown products were found in a resin-like residue of the urine extract. Total methoxyl recovered in 18 hours in the urine was 9-39 per cent. of the amounts ingested. Some was still being excreted at the end of the 18-hour period.

L. E. GILSON (Chem. Abstr.).

Asperula Odorata—Sweet Woodruff. Kreitmair, H. [*Pharmazie*, **4**, 140-1 (1949).]

Brief review of the pharmacology of coumarin and results of sedative and hypnotic studies in mice.

H. A. WEGNER (Chem. Abstr.).

Urethan-induced Damage of the Central Nervous System. Klima, R., and Wengraf, G. [*Wien. med. Wochschr.*, **99**, 109-12 (1949).]

Among 25 patients with blood diseases (leukemia, lymphogranulomatosis, polycythemia) successfully treated with urethan, 8 exhibited psychic and neurological disorders caused by urethan-induced damage to the ganglion cell apparatus of the brain and spinal cord. In 3 autopsies extensive disseminated degenerative foci were found.

ERICH HIRSCHBERG (Chem. Abstr.).

A Suicide by Oral Ingestion of 2, 4-Dinitrophenol. Duquenois, Pierre. [*Ann. med. legale, criminol., police sci., med. sociale et toxicol.*, **30**, 86-91 (1949).]

Ingestion of 1.5 gm. dinitrophenol caused death in about 24 hours. The progressive symptoms of the poisoning are described. Post-mortem analyses showed the presence of aminophenols as well as 2, 4-dinitrophenol in the viscera and urine.

ERICH HIRSCHBERG (Chem. Abstr.).

Effects of a Quaternary Base Capable of Blocking Functions of the Autonomic Nervous System. Longino, F. H., Chittum, J. R., and Grimson, K. S. [*Proc. Soc. Exptl. Biol. Med.*, **70**, 467-75 (1949).]

1, 1-diethyl-2, 6-dimethylpiperidinium bromide, previously described as a ganglionic blocking agent, has an inhibitory or blocking action on functions mediated by the sympathetic and parasympathetic divisions of the autonomic nervous system. In dog and man it reduces blood pressure and prevents several vasomotor reflexes, but does not prevent the vasopressor action of adrenaline. It causes reduction of tone of the stomach and small intestine and abolishes their motor activity, reduces gastric acidity, and causes pupillary dilation, loss of accommodation, and dryness of mucous membranes. Urecholine reverses its effect on gastric motility, and neostigmine appears to reverse all of its effects.

L. E. GILSON (Chem. Abstr.).

Effect of Autonomic Blocking Agents on Sweat Secretion in Cats. Patton, Harry D. [*Proc. Soc. Exptl. Biol. Med.*, **70**, 412-14 (1949).]

Footpad sweat secretion in cats is not blocked by dibenamine, even with doses 3-4 times as great as block sweating in man. Miosis, relaxation of the nictitating membrane and paralysis of the pilomotor system indicated that the dosage was adequate to block known adrenergic systems. Atropine consistently produced complete and irreversible sudomotor paralysis. Apparently the sudomotor inner-

vation in cats is entirely cholinergic and possesses no adrenergic component, as reported in man.

L. E. GILSON (Chem. Abstr.).

Pharmacological Studies on the Causative Agent of Canine Hysteria. Radomski, Jack L., and Woodard, Geoffrey. [*J. Pharmacol. Exptl. Therap.*, **95**, 429-37 (1949); cf. *C. A.*, **42**, 7845c.]

Commercial wheat gluten (80 per cent. protein) treated with 6 gm./kgm. of NCl_3 (agene) was used. Dogs were fed 0.05-2.0 gm./kgm./day. The dose-time curve for production of running fits resembled a hyperbola. The threshold daily dose for cumulative effect was 0.07 gm./kgm./day in dogs (pure bred Dalmatians). The acute toxic dose was 3.5 gm./kgm. for dogs and 10 gm./kgm. for rabbits. The previous administration of agene-treated gluten (I) in doses sufficient to produce ataxia lowered the threshold of reaction to metrazole. This reaction had the characteristics of both canine hysteria and metrazole convulsions. Hydration from forced water intake did not provoke fits in dogs given subeffective doses of (I). Acidosis and alkalosis from administration of NH_4Cl and Na citrate had no effect on production of canine hysteria by (I). Trimethadione and diphenylhydantoin did not suppress canine hysteria, and diphenylhydantoin appeared to potentiate the production of convulsions and death by (I). Daily administration of phenobarbital antagonized the production of canine hysteria.

L. E. GILSON (Chem. Abstr.).

New Data on the Mechanism of Action of Sympathomimetic Substances, in particular Aleudrine. And'yan, A., Lissak, K., and Martin, I. [*Fiziol. Zhur. S.S.S.R.*, **34**, 727-38 (1948).]

Anesthetized cats with both suprarenals tied off were given adrenaline, tyramine, ephedrine, ergotamine, sympathol, adrianol and aleudrine. Action on nictitating membrane and isolated heart was unchanged or enhanced by denervation; aleudrine, in contrast to other sympathomimetic substances, did not contract the nictitating membrane, but relaxed it. Ephedrine caused complete miosis. Ephedrine and tyramine, on the basis of action on the nictitating membrane and heart, act as myotropic rather than neurotropic agents. Positive inotropic and chronotropic action of aleudrine on isolated heart of cat or frog is 10 times stronger than that of adrenaline; no difference in their action on rat heart was observed. Aleudrine has no action on the peripheral circulatory system of a frog, but has a relaxing effect on the virgin cat uterus, which is 10 times stronger than that of adrenaline.

G. M. KOSOLAPOFF (Chem. Abstr.).

Duration of Alcohol Action and Chronaxia. Mouriquand, G., Edel, V., and Chighizola, R. [*Bull. acad. natl. med.*, **133**, 107-12 (1949).]

The chronaxia is lowered in alcohol intoxication. Repeated doses have an additive effect. Return to normal is slower than the elimination from the blood. The nervous system remains for some time sensitized to renewed alcoholic action.

A. E. MEYER (Chem. Abstr.).

